```
=> d his

     (FILE 'HOME' ENTERED AT 19:54:09 ON 13 SEP 2006)

     FILE 'REGISTRY' ENTERED AT 19:54:19 ON 13 SEP 2006
L1             STRUCTURE UPLOADED
L2          50 S L1 SSS SAM

     FILE 'HOME' ENTERED AT 19:55:41 ON 13 SEP 2006

     FILE 'REGISTRY' ENTERED AT 20:03:37 ON 13 SEP 2006
L3             STRUCTURE UPLOADED

     FILE 'HCAPLUS' ENTERED AT 20:04:03 ON 13 SEP 2006

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L4             STRUCTURE UPLOADED
L5          50 S L4 SSS SAM

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L6             STRUCTURE UPLOADED
L7          46 S L6 SSS SAM

     FILE 'HOME' ENTERED AT 20:12:35 ON 13 SEP 2006

     FILE 'REGISTRY' ENTERED AT 20:13:25 ON 13 SEP 2006
L8             STRUCTURE UPLOADED
L9          44 S L8 SSS SAM
L10       1034 S L8 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 20:15:09 ON 13 SEP 2006
L11        252 S L10
               E HYPOCALCEMIA+ALL/CT
               E HYPERCALCEMIA+ALL/CT
               E HYPERPARATHYROIDISM+ALL/CT
L12         34 S L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDIS
L13          9 S L11 AND CALC?
L14          2 S L13 NOT L12

     FILE 'HOME' ENTERED AT 20:24:53 ON 13 SEP 2006

     FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUALINE, AQUIRE, BABS,
     BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CERAB, CIN, COMPENDEX,
     CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT, GENBANK, INSPEC,
     INSPHYS, INVESTEXT, IPA, JICST-EPLUS, KOSMET, ...' ENTERED AT 20:39:35 ON
     13 SEP 2006

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     BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CERAB, CIN, COMPENDEX,
     CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT, GENBANK, INSPEC,
     INSPHYS, INVESTEXT, IPA, JICST-EPLUS, KOSMET, ...' ENTERED AT 20:39:50 ON
     13 SEP 2006

     FILE 'HCAPLUS' ENTERED AT 20:40:08 ON 13 SEP 2006
               SET LINE 250
               SET DETAIL OFF
               E "193275-84-2"/BI,RN 25
               SET NOTICE 1000 SEARCH
L15        175 S E3 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 OR E12 OR E13
               SET NOTICE LOGIN SEARCH
               SET LINE LOGIN
               SET DETAIL LOGIN
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L16      555360 S L15 AND CAL? OR HYPER?
L17          28 S L15 AND (CAL? OR HYPER?)

=> d l17 not l12
L12 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l17 not l12
L18           9 L17 NOT L12

=> s l18 not l13
L19           8 L18 NOT L13

=> d l19 ibib hitstr abs

L19  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:769235  HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER:          145:202934
TITLE:                    Farnesyltransferase inhibitors for treatment of
                          laminopathies, cellular aging and atherosclerosis
INVENTOR(S):              Gordon, Leslie B.; Collins, Francis S.; Glover,
                          Thomas; Glynn, Michael W.; Capell, Brian C.; Cox,
                          Adrienne D.; Der, Channing J.
PATENT ASSIGNEE(S):       United States Dept. of Health and Human Services, USA;
                          Progeria Research Foundation; The Regents of the
                          University of Michigan; The University of North
                          Carolina at Chapel Hill
SOURCE:                   PCT Int. Appl., 104pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006081444         A2    20060803    WO 2006-US2977          20060127
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       US 2005-648307P     P  20050128
                                             US 2005-707192P     P  20050809
IT   193275-84-2, Sarasar
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (farnesyltransferase inhibitors for treatment of laminopathies,
        cellular aging and atherosclerosis)
RN   193275-84-2  HCAPLUS
CN   1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-
     5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-
     (9CI)  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (+).
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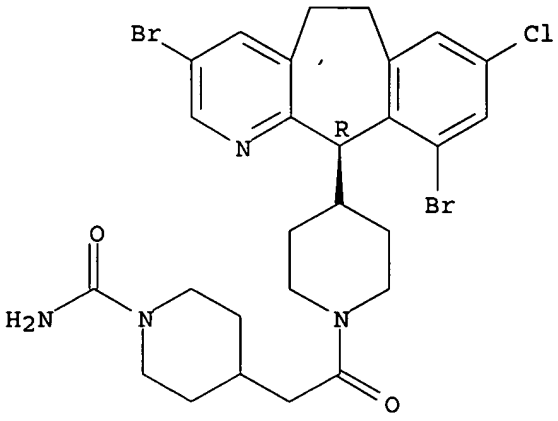
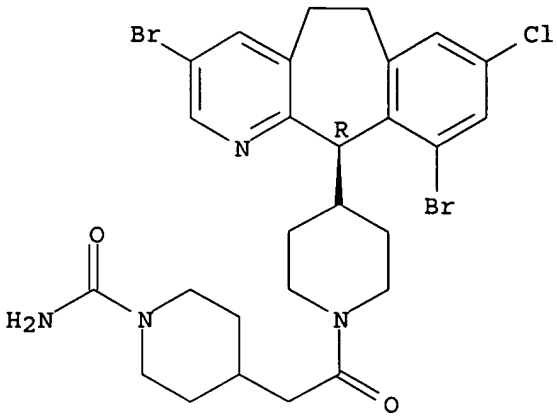


AB Although it can he farnesylated, the mutant lamin A protein expressed in Hutchison-Gilford Progeria Syndrome (HGPS) cannot be defarnesylated because the characteristic mutation causes deletion of a cleavage site necessary for binding the protease ZMPSTE24 and effecting defarnesylation. The result is an aberrant farnesylated protein (called "progerin") that alters normal lamin A function as a dominant neg., as well as assuming its own aberrant function through its association with the nuclear membrane. The retention of farnesylation, and potentially other abnormal properties of progerin and other abnormal lamin gene protein products, produces disease. Farnesyltransferase inhibitors (FTIs) (both direct effectors and indirect inhibitors) will inhibit the formation of progerin, cause a decrease in lamin A protein, and/or an increase prelamin A protein. Decreasing the amount of aberrant protein improves cellular effects caused by and progerin expression. Similarly, treatment with FTIs should improve disease status in progeria and other laminopathies. In addition, elements of atherosclerosis and aging in non-laminopathy individuals will improve after treatment with farnesyltransferase inhibitors.

=> d l19 ibib hitstr abs 2-8

L19 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:196534 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 145:23059
TITLE: A rapid and simple HPLC-UV method for the determination of inhibition characteristics of farnesyl transferase inhibitors
AUTHOR(S): Appels, Natalie M. G. M.; Tung, Kien-On; Rosing, Hilde; Schellens, Jan H. M.; Beijnen, Jos H.
CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.
SOURCE: Biomedical Chromatography (2006), 20(2), 161-165
CODEN: BICHE2; ISSN: 0269-3879
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 193275-84-2, Lonafarnib
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl transferase inhibitor screening by HPLC-UV)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Ras proteins play an important role in the development of cancer. Farnesyl transferase inhibitors (FTIs) block the first obligatory post-translational step for activation, prenylation, of Ras proteins. To find new potent FTIs, rapid enzyme activity assays are required to reduce FTI development time. Most assays to date are based on radioactive labeled substrates. We developed a new, in vitro, farnesyl transferase assay based on gradient chromatog. coupled to UV detection. Unfarnesylated and farnesylated H-Ras proteins were resolved on a C18 wide-pore HPLC column and their concns. were determined with use of a calibration curve of unfarnesylated H-Ras. The assay was used to investigate inhibition characteristics of FTIs. The IC50 values of the FTIs L778,123 and SCH66336 were 4.2 nM and 78 μM, resp. This assay could support the screening and development of FTIs to obtain rapid insights into their inhibitory properties.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:490384 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 143:42681
TITLE: Anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer
INVENTOR(S): Wang, Yan; Pachter, Jonathan A.; Bishop, Walter R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005052005	A1	20050609	WO 2004-US38842	20041119

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004292554	A1	20050609	AU 2004-292554	20041119
US 2005136063	A1	20050623	US 2004-993395	20041119
EP 1689782	A1	20060816	EP 2004-811545	20041119

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU

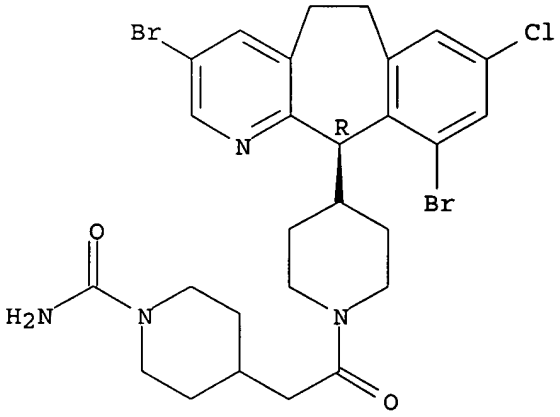
PRIORITY APPLN. INFO.: US 2003-524732P P 20031121
WO 2004-US38842 W 20041119

IT 193275-84-2, Lonafarnib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



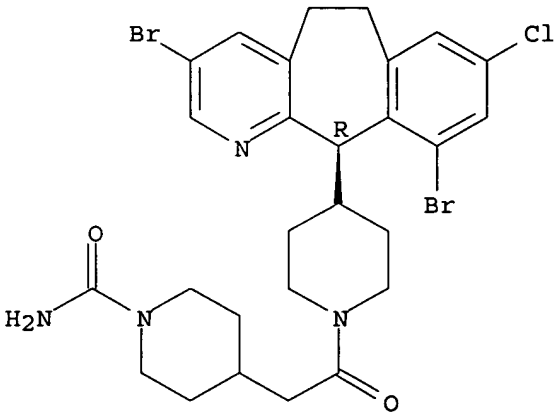
AB The present invention provides combinations including a binding composition, such as an anti-IGFR1 antibody, in association with a chemotherapeutic agent. The antibody is e.g. a human monoclonal antibody recognizing human IGFR-1, especially soluble IGFR-1. The chemotherapeutic agent is selected from a taxane, topoisomerase inhibitor, signal transduction inhibitor, cell cycle inhibitor, farnesyl protein transferase inhibitor, EGFR inhibitor, HER2 inhibitor, VEGFR inhibitor, MAP kinase inhibitor, MEK kinase inhibitor, AKT kinase inhibitor, mTOR inhibitor, etc. Methods for using the combinations to treat medical conditions, such as cancer, are also provided.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:369627 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 141:388236
TITLE: Phase I study of the farnesyltransferase inhibitor lonafarnib with paclitaxel in solid tumors
AUTHOR(S): Khuri, Fadlo R.; Glisson, Bonnie S.; Kim, Edward S.; Statkevich, Paul; Thall, Peter F.; Meyers, Michael L.; Herbst, Roy S.; Munden, Reginald F.; Tendler, Craig; Zhu, Yali; Bangert, Sandra; Thompson, Elizabeth; Lu, Charles; Wang, Xue-Mei; Shin, Dong M.; Kies, Merrill S.; Papadimitrakopoulou, Vali; Fossella, Frank V.;

Kirschmeier, Paul; Bishop, W. Robert; Hong, Waun Ki
CORPORATE SOURCE: Winship Cancer Institute, Emory University, Atlanta, GA, 30322, USA
SOURCE: Clinical Cancer Research (2004), 10(9), 2968-2976
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 193275-84-2, Lonafarnib
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recommended dose of farnesyltransferase inhibitor lonafarnib was 100mg p.o. twice daily with 175 mg/m2 of paclitaxel i.v. every three weeks in patients with solid tumors and encouraging clin. activity observed with combination regimen)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



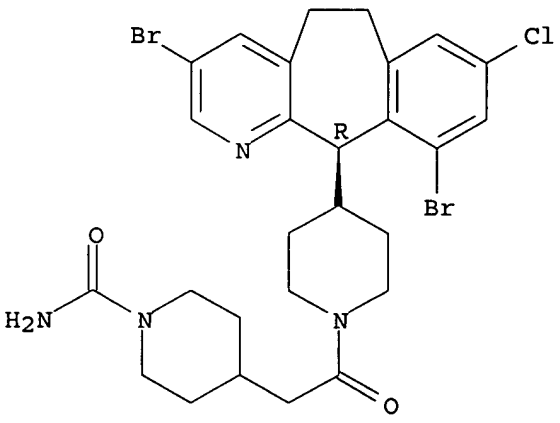
AB To establish the maximum tolerated dose of lonafarnib, a novel farnesyltransferase inhibitor, in combination with paclitaxel in patients with solid tumors and to characterize the safety, tolerability, dose-limiting toxicity, and pharmacokinetics of this combination regimen. In a Phase I trial, lonafarnib was administered p.o., twice daily (b.i.d.) on continuously scheduled doses of 100 mg, 125 mg, and 150 mg in combination with i.v. paclitaxel at doses of 135 mg/m2 or 175 mg/m2 administered over 3 h on day 8 of every 21-day cycle. Plasma paclitaxel and lonafarnib concns. were collected at selected time points from each patient. Twenty-four patients were enrolled; 21 patients were evaluable. The principal grade 3/4 toxicity was diarrhea (5 of 21 patients), which was most likely due to lonafarnib. dose-limiting toxicities included grade 3 hyperbilirubinemia at dose level 3 (100 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel); grade 4 diarrhea and grade 3 peripheral neuropathy at dose level 3A (125 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel); and grade 4 neutropenia with fever and grade 4 diarrhea at level 4 (150 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel). The maximum tolerated dose established by the continual reassessment method was lonafarnib 100 mg b.i.d. and paclitaxel 175 mg/m2. Paclitaxel appeared to have no effect on the pharmacokinetics of lonafarnib. The median duration of therapy was eight cycles, including seven cycles with paclitaxel. Six of 15 previously treated patients had a durable partial response, including 3 patients who had previous taxane therapy. Notably, two of five patients with taxane-resistant metastatic non-small cell lung cancer

had partial responses. When combined with paclitaxel, the recommended dose of lonafarnib for Phase II trials is 100 mg p.o. twice daily with 175 mg/m2 of paclitaxel i.v. every 3 wk. Addnl. studies of lonafarnib in combination regimens appear warranted, particularly in patients with non-small cell lung cancer.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:145717 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 141:184712
TITLE: In vitro study of farnesyltransferase inhibitor SCH 66336, in combination with chemotherapy and radiation, in non-small cell lung cancer cell lines
AUTHOR(S): Loprevite, Maura; Favoni, Roberto E.; De Cupis, Alessandra; Scolaro, Tindaro; Semino, Claudia; Mazzanti, Paola; Ardizzoni, Andrea
CORPORATE SOURCE: Medical Oncology A, Unit, National Institute for Cancer Research, Genoa, I-16132, Italy
SOURCE: Oncology Reports (2004), 11(2), 407-414
CODEN: OCRPEW; ISSN: 1021-335X
PUBLISHER: Oncology Reports
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 193275-84-2, SCH 66336
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FTi SCH 66336 showed dose dependent cytostatic antitumor activity and dose dependent synergism in combination with antimitotic agent paclitaxel in NSCLC cell lines A-549, LX-1, CaLu-6 in vitro)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB K-ras alterations have been reported in 20-30% of non-small cell lung cancer (NSCLC) and represent a suitable target for the development of novel anticancer agents, such as Farnesyl transferase inhibitors (FTi), a new class of agents inhibiting the post-translational modification of the K-ras proteins. The effectiveness of FTi SCH66336 in inhibiting cell proliferation and deranging cell cycle of NSCLC cell lines as well as its interaction with chemotherapy or radiation have been evaluated. The activity of FTi SCH66336, alone or in combination with paclitaxel, gemcitabine, and radiotherapy, was examined in 3 cell lines, A-549, LX-1 and

CaLu-6, by colorimetric MTT assay. Cell cycle perturbation and apoptosis were also assessed by cytofluorimetric anal. The activity of SCH 66336 was found to be concentration- and time-dependent. The effect of SCH 66336, as demonstrated by cell growth recovery expts., resulted cytostatic and it was superimposable in both cell lines bearing 2 different K-ras mutations (A-549 and LX-1) and in K-ras wild-type Ca-Lu-6. In all cell lines the combination of SCH 66336 and paclitaxel resulted in a synergism of action when SCH 66336 followed paclitaxel treatment, whereas, antagonism was found when SCH 66336 preceded paclitaxel treatment. No significant synergism or addition with SCH 66336 followed by radiation treatment was noted. Different cell cycle phase blocks at various drug concns. were observed In conclusion, SCH 66336 displays concentration-dependent cytostatic antitumor activity and schedule-dependent synergy with 2 commonly used anticancer agents in NSCLC cell lines. Further clin. testing of these combinations is warranted.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

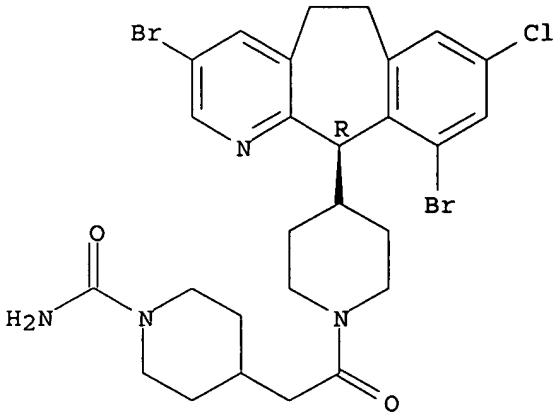
L19 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:314549 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 132:343356
TITLE: A prenyl-protein transferase inhibitor for treating endometriosis
INVENTOR(S): Oliff, Allen I.; Gibbs, Jackson B.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 365 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025789	A1	20000511	WO 1999-US25001	19991025

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-106179P P 19981029
GB 1999-160 A 19990105
OTHER SOURCE(S): MARPAT 132:343356
IT 193275-84-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein prenyltransferase inhibitors for treatment of endometriosis and related disorders)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

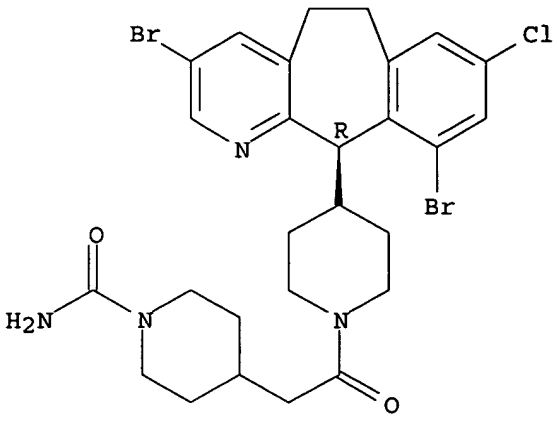
Absolute stereochemistry. Rotation (+).



AB A method of preventing and treating endometriosis, uterine fibroids, dysfunctional uterine bleeding and endometrial hyperplasia is disclosed which is comprised of administering to a mammalian patient in need of such treatment an effective amount of a prenyl-protein transferase inhibitor. Various in vitro inhibition assays for farnesyltransferase were developed and effect of a prenyl-protein transferase inhibitor (5-160 mg/kg/day) was evaluated in vitro in the rat model of endometriosis.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

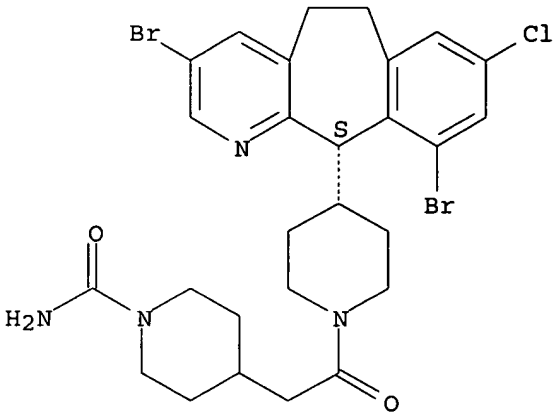
L19 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:337641 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 131:124925
TITLE: Tricyclic Farnesyl Protein Transferase Inhibitors: Crystallographic and Calorimetric Studies of Structure-Activity Relationships
AUTHOR(S): Strickland, Corey L.; Weber, Patricia C.; Windsor, William T.; Wu, Zhen; Le, Hung V.; Albanese, Margaret M.; Alvarez, Carmen S.; Cesarz, David; del Rosario, Joycelyn; Deskus, Jeffrey; Mallams, Alan K.; Njoroge, F. George; Piwinski, John J.; Remiszewski, Stacy; Rossman, Randall R.; Taveras, Arthur G.; Vibulbhan, Bancha; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Ganguly, Ashit K.
CORPORATE SOURCE: Departments of Structural Chemistry and Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(12), 2125-2135
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 193275-84-2, SCH 66336 193275-85-3
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(tricyclic farnesyl protein transferase inhibitors and crystallog. and calorimetric studies of structure-activity relationships)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 193275-85-3 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AB Crystallog. and thermodn. studies of farnesyl protein transferase (FPT) complexed with novel tricyclic inhibitors provide insights into the observed SAR for this unique class of nonpeptidic FPT inhibitors. The crystallog. structures reveal a binding pattern conserved across the mono-, di-, and trihalogen series. In the complexes, the tricycle spans the FPT active site cavity and interacts with both protein atoms and the isoprenoid portion of bound farnesyl diphosphate. An amide carbonyl, common to the tricyclic compds. described here, participates in a water-mediated hydrogen bond to the protein backbone. Ten high-resolution crystal structures of inhibitors complexed with FPT are reported. Included are crystallog. data for FPT complexed with SCH 66336, a compound currently undergoing clin. trials as an anticancer agent (SCH 66336, 4-[2-[4-(3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl)-1-piperidinyl]-2-oxoethyl]-1-piperidinecarboxamide). Thermodn. binding parameters show favorable enthalpies of complex formation and small net entropic contributions as observed for 4-[2-[4-(3,10-dibromo-8-chloro-6,11-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidinyl]-2-oxoethyl]pyridine N-oxide where $\Delta H°bind$ = -12.5 kcal/mol and $T\Delta S°bind$ = -1.5 kcal/mol.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:564267 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 129:197984
TITLE: Combined tumor suppressor gene therapy and chemotherapy in the treatment of neoplasms
INVENTOR(S): Nielsen, Loretta; Horowitz, Jo Ann; Maneval, Daniel C.; Demers, G. William; Rybak, Mary Ellen; Resnick, Gene
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

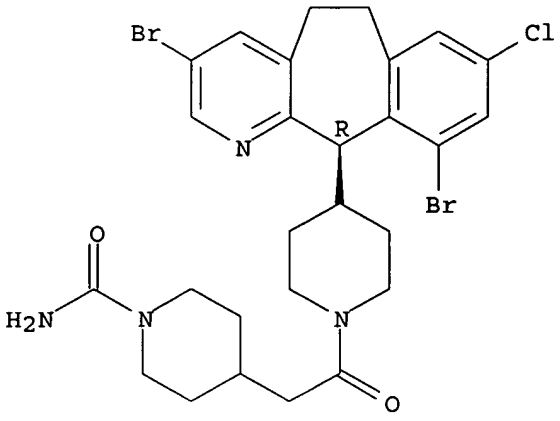
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9835554	A2	19980820	WO 1998-US3514	19980217
WO 9835554	A3	19981126		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2282683	AA	19980820	CA 1998-2282683	19980217
AU 9864380	A1	19980908	AU 1998-64380	19980217
AU 737621	B2	20010823		
EP 969720	A2	20000112	EP 1998-910038	19980217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 337283	A	20010223	NZ 1998-337283	19980217
JP 2001511815	T2	20010814	JP 1998-536033	19980217
BR 9807418	A	20020122	BR 1998-7418	19980217
US 2003060434	A1	20030327	US 1999-311772	19990513
NO 9903943	A	19991015	NO 1999-3943	19990817
US 2003064949	A1	20030403	US 2002-86294	20020228
US 2004235736	A1	20041125	US 2004-824058	20040413
US 2005142112	A1	20050630	US 2004-823932	20040413

PRIORITY APPLN. INFO.:

US 1997-38065P	P	19970218
US 1997-801285	A	19970218
US 1997-801681	A	19970218
US 1997-801755	A	19970218
US 1997-801765	A	19970218
US 1997-47834P	P	19970528
US 1998-24932	B1	19980217
WO 1998-US3514	W	19980217
US 1999-311772	B3	19990513

IT 193275-84-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor suppressor gene therapy-chemotherapy combination for treatment of neoplasms and hyperproliferative cells)
RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB In one embodiment, the invention provides methods of treating mammalian cancer or hyperproliferative cells, the method comprising contacting the cells with a tumor suppressor protein or tumor suppressor nucleic acid and also contacting the cells with at least one adjunctive anticancer agent. The invention also provides for a pharmacol. composition comprising a tumor suppressor protein or a tumor suppressor nucleic acid and at least one adjunctive anti-cancer agent, as well as a kit for the treatment of mammalian cancer or hyperproliferative cells.

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	167.82	178.76

FILE 'HCAPLUS' ENTERED AT 20:15:09 ON 13 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Sep 2006 VOL 145 ISS 12
FILE LAST UPDATED: 12 Sep 2006 (20060912/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L11        252 L10

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"Endocrine system, disease" OR "Parathyroid gland, disease" OR "Calcium" or (bon? metast?) or
PTH or calcitonin or granulomatous or sarcoidosis or calcitriol or (hematologic malignancy)
or lymphopro?)
          3125 HYPOCALCEMIA
             7 HYPOCALCEMIAS
          3131 HYPOCALCEMIA
                 (HYPOCALCEMIA OR HYPOCALCEMIAS)
          5273 HYPERCALCEMIA
            27 HYPERCALCEMIAS
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                 (HYPERCALCEMIA OR HYPERCALCEMIAS)
          4337 HYPERPARATHYROIDISM
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          4337 HYPERPARATHYROIDISM
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        885305 "DISEASE"
        240606 "DISEASES"
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                 ("DISEASE" OR "DISEASES")
       1292203 "ANIMAL"
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       1627620 "ANIMAL"
                 ("ANIMAL" OR "ANIMALS")
         28970 "DISEASE, ANIMAL"
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         68108 "ENDOCRINE"
           366 "ENDOCRINES"
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                 ("ENDOCRINE" OR "ENDOCRINES")
       2319186 "SYSTEM"
       1270331 "SYSTEMS"
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        885305 "DISEASE"
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                ("DISEASE" OR "DISEASES")
          2223 "ENDOCRINE SYSTEM, DISEASE"
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         21676 "PARATHYROID"
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        313902 "GLAND"
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        885305 "DISEASE"
        240606 "DISEASES"
        994202 "DISEASE"
                ("DISEASE" OR "DISEASES")
           238 "PARATHYROID GLAND, DISEASE"
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         16508 CALCITONIN
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                (CALCITONIN OR CALCITONINS)
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          2154 SARCOIDOSIS
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         21351 HEMATOL
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                (MALIGNANCY OR MALIGNANCIES)
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          4952 LYMPHOPRO?
L12         34 L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDISM
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              ROID GLAND, DISEASE" OR "CALCIUM" OR (BON? METAST?) OR PTH OR
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              TOLOGIC MALIGNANCY) OR LYMPHOPRO?)

=> d l12 scan

L12   34 ANSWERS   HCAPLUS  COPYRIGHT 2006 ACS on STN
IC   ICM  A61K031-59
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INCL 514167000
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
TI Methods of using vitamin D compounds in the treatment of myelodysplastic syndromes
ST vitamin D compd treatment myelodysplastic syndrome; calcitriol treatment myelodysplastic syndrome
IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-10, MIGLYOL 812; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Suspensions
(agent for making, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Thiols, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antithymocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Antifoaming agents
Antioxidants
Binders
Buffers
Chelating agents
Coloring materials
Fillers
Flavoring materials
Lubricants
Odor and Odorous substances
Opacifiers
Plasticizers
Preservatives
Thickening agents
(as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Cytotoxic agents
Immunomodulators
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Cytokines
Growth factors, animal
Hemopoietins
Interleukin 1
Interleukin 11
Interleukin 12
Interleukin 2
Interleukin 3
Interleukin 6
Interleukin 8
Tocopherols
Transcription factors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of

myelodysplastic syndromes)
IT Drug delivery systems
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(depsipeptides, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Tackifiers
(detackifiers, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Signal transduction, biological
(inhibitors, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug delivery systems
(injections, i.v.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Viscosity
(modulators, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Stability
(of calcitriol capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Solvates
Stereoisomers
(of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug delivery systems
(prodrugs, of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug targets
(related to MDS, agents binding to, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Amines, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiol, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Combination chemotherapy
Human
Myelodysplastic syndromes
(vitamin D compds. in treatment of myelodysplastic syndromes)
IT Interferons
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT 127464-60-2, VEGF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-VEGF, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT 50-02-2, Dexamethasone 50-35-1, Thalidomide 53-03-2, Prednisone 147-94-4, Cytarabine 148-82-3, Melphalan 302-79-4, Retinoic acid 320-67-2, 5-Azacytidine 863-61-6, Menatetrenone 1327-53-3, Arsenic

trioxide 1406-18-4D, Vitamin E, derivs. 2353-33-5, Decitabine
4346-18-3, Phenyl butyrate 4759-48-2 6493-05-6, Pentoxifylline
9002-96-4, Vitamin E TPGS 9014-42-0, Thrombopoietin 11096-26-7, EPO
11103-57-4D, Vitamin A, derivs. 12001-79-5D, Vitamin K, derivs.
20537-88-6, Amifostine 20830-81-3, Daunorubicin 21679-14-1,
Fludarabine 33419-42-0, Etoposide 58957-92-9, Idarubicin 59865-13-3,
Cyclosporin A 65271-80-9, Mitoxantrone 83869-56-1, GM-CSF
123948-87-8, Topotecan 143011-72-7, Granulocyte-colony stimulating
factor 185243-69-0, TNFR:Fc 192185-72-1, ZARNESTRA 193275-84-2
, SARASAR 204005-46-9, SU5416 212142-18-2 220578-59-6, Gemtuzumab
ozogamicin 252916-29-3, SU6668
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of
myelodysplastic syndromes)
IT 32222-06-3, Calcitriol
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(as vitamin D compound; vitamin D compds. in treatment of myelodysplastic
syndromes)
IT 7440-38-2, Arsenic, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compound containing, as addnl. active agent; vitamin D compds. in treatment
of myelodysplastic syndromes)
IT 1406-16-2D, Vitamin D, compds.
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D compds. in treatment of myelodysplastic syndromes)
IT 128-37-0, Butylated hydroxytoluene, biological studies 25013-16-5,
Butylated hydroxyanisole 121548-04-7, Gelucire 44/14
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D compds. in treatment of myelodysplastic syndromes)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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(FILE 'HOME' ENTERED AT 19:54:09 ON 13 SEP 2006)

FILE 'REGISTRY' ENTERED AT 19:54:19 ON 13 SEP 2006
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FILE 'HOME' ENTERED AT 19:55:41 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:03:37 ON 13 SEP 2006
L3 STRUCTURE UPLOADED

FILE 'HCAPLUS' ENTERED AT 20:04:03 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:04:13 ON 13 SEP 2006
L4 STRUCTURE UPLOADED
L5 50 S L4 SSS SAM

FILE 'HOME' ENTERED AT 20:05:51 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:09:46 ON 13 SEP 2006
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L7 46 S L6 SSS SAM

FILE 'HOME' ENTERED AT 20:12:35 ON 13 SEP 2006

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L10        1034 S L8 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 20:15:09 ON 13 SEP 2006
L11         252 S L10
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                E HYPERCALCEMIA+ALL/CT
                E HYPERPARATHYROIDISM+ALL/CT
L12          34 S L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDIS

=> d l12 ibib abs hitstr

L12  ANSWER 1 OF 34  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:608613  HCAPLUS
DOCUMENT NUMBER:          145:83394
TITLE:                    Piperazine derivatives as farnesyl protein transferase
                          inhibitors and their preparation, pharmaceutical
                          compositions and methods for treating proliferative
                          diseases
INVENTOR(S):              Mallams, Alan K.
PATENT ASSIGNEE(S):       Schering Corporation, USA
SOURCE:                   PCT Int. Appl., 337 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     WO 2006065794         A1    20060622    WO 2005-US45019        20051212
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
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             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       US 2004-636451P     P  20041214
OTHER SOURCE(S):          MARPAT 145:83394
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are compds. of the formula I and their pharmaceutically acceptable salts. Compds. of formula I wherein dotted lines is optional double bonds; a, b, c and d is CR1; one of a, b, c and d are N or N+O-; R1, R3 and R4 are independently is H, halo, CF3, OH and derivs., CHO, acyl, S(O)tH and derivs., NH2 and derivs., NO2, CO2H and derivs., CN, etc.; t is 0, 1 or 2; R4R4 taken together represent a (un)saturated C5-7 fused ring to the benzene ring; R5, R6 and R7 are independently H, CF3, CHO, acyl, (un)substituted alkyl, or (un)substituted aryl; X is N, CH, or C; A and B are independently absent, Hm alkyl, aryl, aralkyl, OH and derivs., OCO2H and derivs., OCHO, and O-acyl, etc.; R8 when X is CH or C is H,

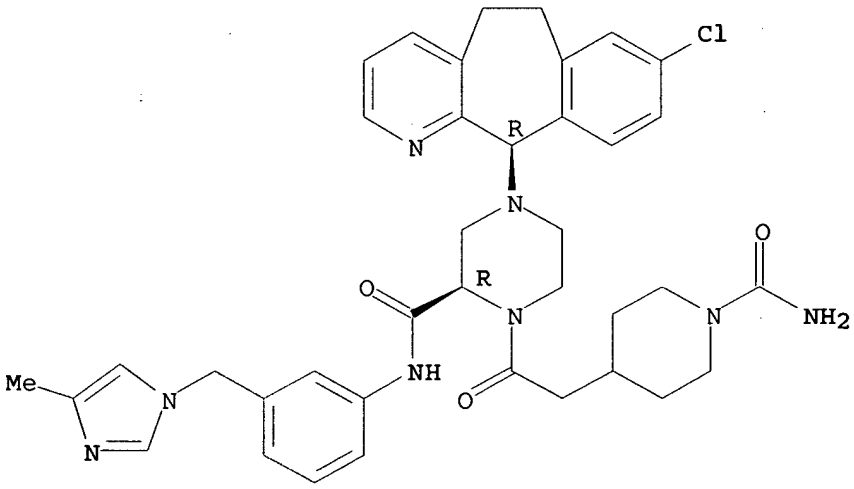
COYR12 or SO2R13; R8 when X is N is H, COTR12, SO2R13 or a tricyclic ring system, etc; R9 is halo, (un)substituted alkyl, trifluoroalkyl, HO, alkyloxy, amino or acylamino; R11 is H, alkyl, or arylalkyl; Y is (un)substituted methylene or NH; R12 is (un)substituted (hetero)(cyclo)alkyl, or (un)substituted (hetero)aryl(alkyl); R13 is (un)substituted (cyclo)alkyl or(un)substituted (aryl)alkyl; R16 is unsubstituted imidazole; m us 0 to 4; n is 1, 2, 3 or 4; and their pharmaceutically acceptable salts are claimed. Also disclosed are uses of the compds. of formula Ifor the manufacture of a medicament for treating cancer and for inhibiting farnesyl protein transferase. Example compound II was prepared by amidation of compound III with 1-(3-aminobenzyl)imidazole to give racemic compound II was separated by chiral HPLC to give the enantiomerically enriched compound II. All the invention compds. were evaluated for their farnesyl protein transferase inhibitory activity. From the assay, it was determined that most of the tested compds. exhibited good IC50 values in the range of < 0.05 nM to about 200 nM.

IT 892392-87-9P 892392-96-0P 892393-02-1P
892393-03-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazine derivs. as farnesyl protein transferase inhibitors useful in treatment of cancer and other proliferative diseases)

RN 892392-87-9 HCAPLUS

CN 2-Piperazinecarboxamide, 1-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-4-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-[(4-methyl-1H-imidazol-1-yl)methyl]phenyl]-, (2R)- (9CI) (CA INDEX NAME)

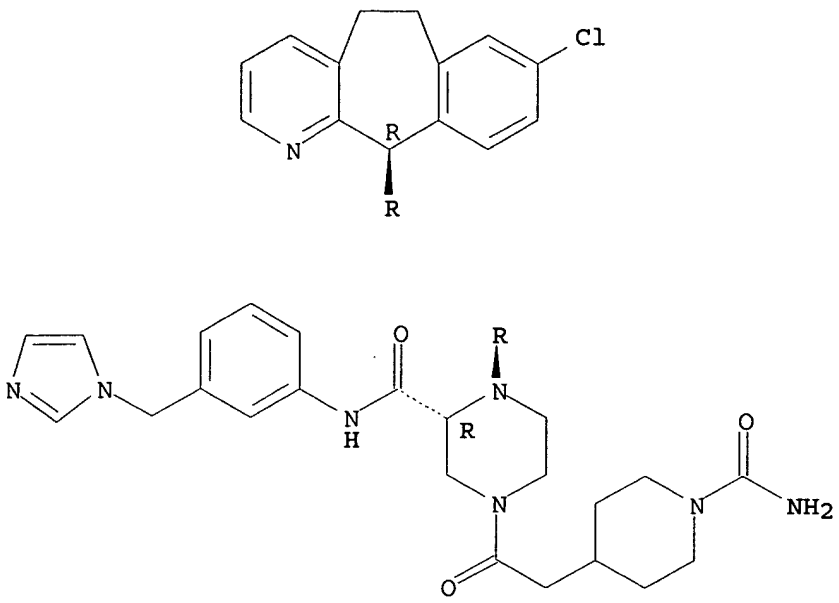
Absolute stereochemistry. Rotation (+).



RN 892392-96-0 HCAPLUS

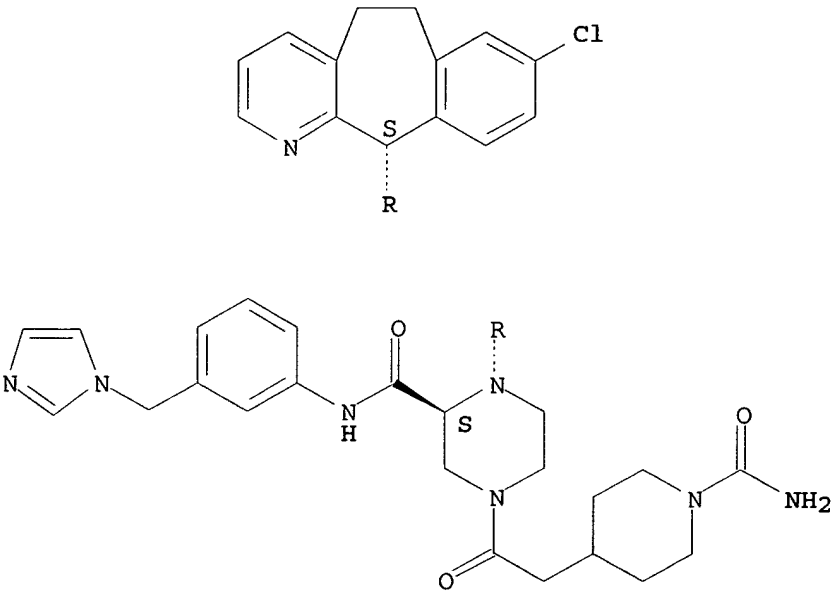
CN 2-Piperazinecarboxamide, 4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



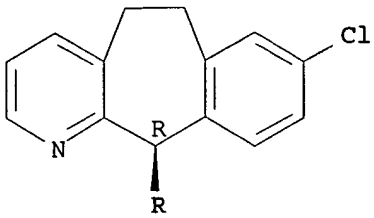
RN 892393-02-1 HCAPLUS
CN 2-Piperazinecarboxamide, 4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11S)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2S)- (9CI) (CA INDEX NAME)

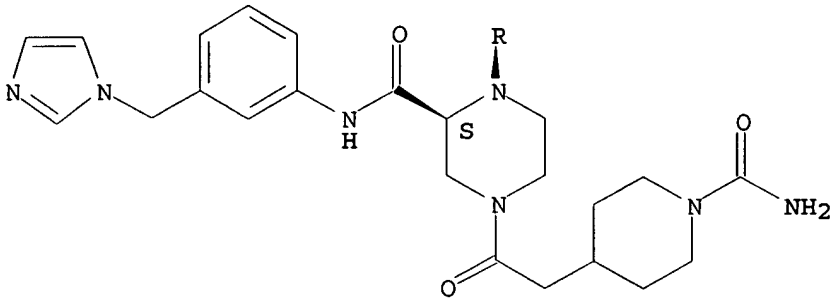
Absolute stereochemistry. Rotation (-).



RN 892393-03-2 HCAPLUS
CN 2-Piperazinecarboxamide, 4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).





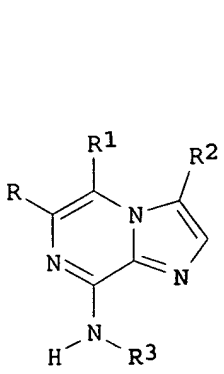
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l12 ibib abs hitstr 2-32

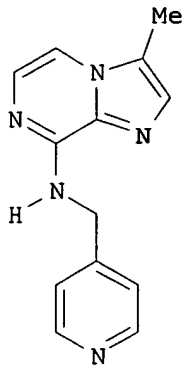
L12 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:463553 HCAPLUS
DOCUMENT NUMBER: 144:488677
TITLE: Preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors
INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Zhao, Lianyun; Curran, Patrick J.; Belanger, David B.; Hamann, Blake; Reddy, Panduranga A.; Siddiqui, M. Arshad
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 161 pp., Cont.-in-part of U.S. Ser. No. 47,524.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006106023	A1	20060518	US 2005-272392		20051110
US 2004063715	A1	20040401	US 2003-665005		20030919
US 6919341	B2	20050719			
US 2005130980	A1	20050616	US 2005-47524		20050131
PRIORITY APPLN. INFO.:			US 2002-412997P	P	20020923
			US 2003-665005	A3	20030919
			US 2005-47524	A2	20050131

OTHER SOURCE(S): MARPAT 144:488677
GI



I



II

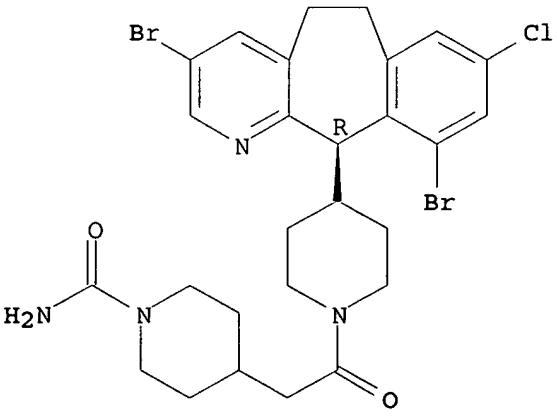
AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R1 = H, halo or alkyl; R2 = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R3 = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-a]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC50 value of 22.5 μM.

IT 193275-84-2, SCH 66336
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



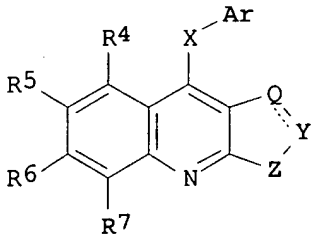
L12 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:366977 HCAPLUS
DOCUMENT NUMBER: 144:412498
TITLE: Preparation of substituted N-aryl-1H-pyrazolo[3,4-b]quinolin-4-amines and analogs as activators of

caspases and inducers of apoptosis
INVENTOR(S): Zhang, Han-Zhong; Cai, Sui Xiong; Drewe, John A.
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041900	A2	20060420	WO 2005-US35793	20051006
WO 2006041900	A3	20060713		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-616539P P 20041007
OTHER SOURCE(S): MARPAT 144:412498
GI



I

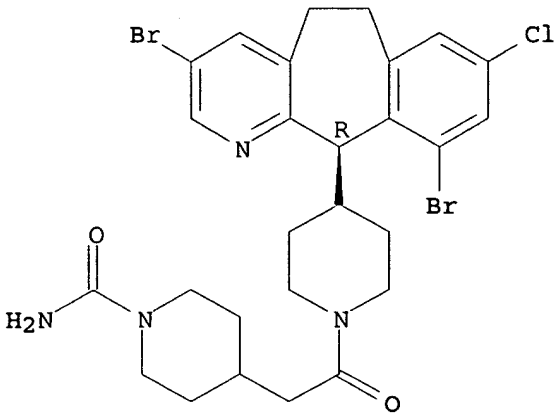
AB The title compds. I [X = O, NR3, S, SO, SO2; Ar = (un)substituted aryl, heteroaryl, carbocyclyl, etc.; Q = CR2, CR12R13; Y = N, CR10R11; Z = NR1, CR8R9; R1, R3 = H, (un)substituted alkyl; R2, R4-R13 = H, halo, aryl, etc.] which are activators of caspases and inducers of apoptosis and therefore can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs (biol. data given), were prepared E.g., a multi-step synthesis of 1,3-dimethyl-N-[4-(methoxycarbonyl)phenyl]-1H-pyrazolo[3,4-b]quinolin-4-amine, starting from anthranilic acid and 4-methyleneoxetan-2-one, was given. Pharmaceutical composition comprising the compound I alone or in combination with other therapeutic agents are disclosed.

IT 193275-84-2, SCH66336
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted N-aryl-1H-pyrazolo[3,4-b]quinolin-4-amines and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:317333 HCAPLUS
DOCUMENT NUMBER: 144:363075
TITLE: Use of inhibitors of 24-hydroxylase in combination with other agents for the treatment of cancer
INVENTOR(S): Polvino, William J.
PATENT ASSIGNEE(S): Sapphire Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006036892	A2	20060406	WO 2005-US34410	20050923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006078494	A1	20060413	US 2005-234552	20050923
PRIORITY APPLN. INFO.:			US 2004-612712P P	20040924
OTHER SOURCE(S):	MARPAT 144:363075			

AB The invention discloses a method for treating cancer in a subject. The method comprises administering to a subject suffering from cancer a therapeutically effective amount of a 24-hydroxylase inhibitor in combination with a second amount of a suitable cancer therapeutic. The 24-hydroxylase inhibitor can be coadministered with a chemotherapeutic agent, such an antitumor antibiotic (e.g., mitoxantrone or bleomycin), an alkylating agent (e.g., estramustine or melphalan), a plant alkaloid (e.g., taxanes such as paclitaxel or docetaxel or viva alkaloids such as vincristine or vinblastine) or a combination thereof. In addnl. therapy, the 24-hydroxylase inhibitor can be coadministered as an adjuvant to

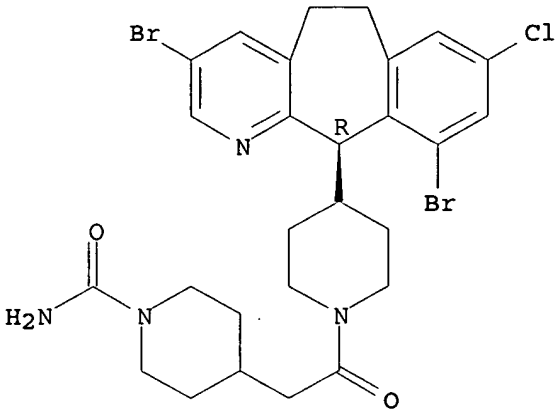
radiation therapy, such as an external beam irradiation or a radioisotope therapy, such as radiopharmaceutical therapy. Further, the 24-hydroxylase inhibitor can be coadministered as part of a combination therapy that includes hormonal ablation.

IT 193275-84-2, Lonafarnib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D 24-hydroxylase inhibitor combination with other agent for treatment of cancer)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:98364 HCAPLUS

DOCUMENT NUMBER: 144:460150

TITLE: Farnesyl transferase inhibitors

AUTHOR(S): Basso, Andrea D.; Kirschmeier, Paul; Bishop, W. Robert

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Lipid Research (2006), 47(1), 15-31
CODEN: JLPRAW; ISSN: 0022-2275

PUBLISHER: American Society for Biochemistry and Molecular Biology, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Some proteins undergo posttranslational modification by the addition of an isoprenyl lipid (farnesyl- or geranylgeranyl-isoprenoid) to a cysteine residue proximal to the C terminus. Protein isoprenylation promotes membrane association and contributes to protein-protein interactions. Farnesylated proteins include small GTPases, tyrosine phosphatases, nuclear lamina, cochaperones, and centromere-associated proteins. Prenylation is required for the transforming activity of Ras. Because of the high frequency of Ras mutations in cancer, farnesyl transferase inhibitors (FTIs) were investigated as a means to antagonize Ras function. Evaluation of FTIs led to the finding that both K- and N-Ras are alternatively modified by geranylgeranyl prenyltransferase-1 in FTI-treated cells. Geranylgeranylated forms of Ras retain the ability to associate with the plasma membrane and activate substrates. Despite this, FTIs are effective at inhibiting the growth of human tumor cells in vitro, suggesting that activity is dependent on blocking the farnesylation of other proteins. FTIs also inhibit the in vivo growth of human tumor xenografts and sensitize these models to chemotherapeutics, most notably

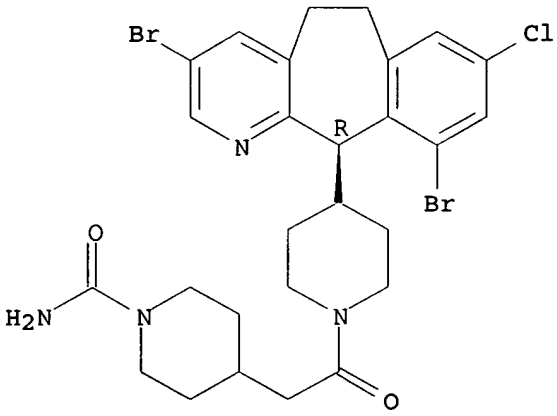
taxanes. Several FTIs have entered clin. trials for various cancer indications. In some clin. settings, primarily hematol. malignancies, FTIs have displayed evidence of single-agent activity. Clin. studies in progress are exploring the antitumor activity of FTIs as single agents and in combination. This review will summarize the basic biol. of FTIs, their antitumor activity in preclin. models, and the current status of clin. studies with these agents.

IT 193275-84-2, Lonafarnib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl transferase inhibitors)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 220 THERE ARE 220 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:40315 HCAPLUS
DOCUMENT NUMBER: 144:460119
TITLE: Farnesyltransferase inhibitors in myelodysplastic syndrome
AUTHOR(S): Feldman, E. J.
CORPORATE SOURCE: Weill Medical College, Cornell University, New York, NY, 10021, USA
SOURCE: Current Hematology Reports (2005), 4(3), 186-190
CODEN: CHRUEI; ISSN: 1540-3408
PUBLISHER: Current Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The farnesyltransferase inhibitors (FTIs) are in active clin. development in a variety of human malignancies. The most promising activity to date has been demonstrated in patients with hematol. malignancies, in particular acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). In patients with MDS, two non-peptido-mimetic agents, tipifarnib (Zarnestra, Johnson & Johnson, New Brunswick, NJ) and Ionafarnib (Sarasar, Schering-Plough, Kenilworth, NJ) have been the most extensively studied. In both phase I and phase II trials, tipifarnib has demonstrated significant efficacy with overall response rates of 30%, with complete remissions in about 15%. Dose-limiting side effects have been primarily myelosuppression, although fatigue, neurotoxicity, and occasional renal dysfunction have required

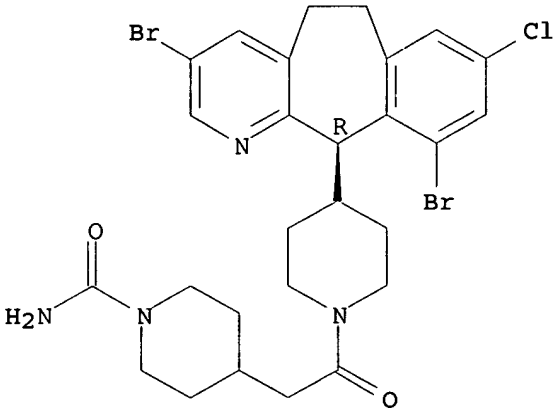
dose redns. Lonafarnib in patients with MDS has also resulted in clin. responses in approx. 30%, including significant improvements in platelet counts. Lonafarnib has been associated with primarily diarrhea and other gastrointestinal toxicity, anorexia, and nausea, which has limited its efficacy. Clin. response correlation with documentation of inhibition of farnesyltransferase and/or evidence of decreased farnesylation of downstream protein targets has not been demonstrated with either agent. In addition, the presence of an activating Ras mutation has not predicted response to therapy with FTIs in MDS and AML. Despite this, significant clin. efficacy of the FTIs in MDS, on par with that of currently available chemotherapeutic agents, has been observed, leading to further development of this new class of drugs in MDS and AML.

IT 193275-84-2, Sarasar
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase I and II trial of FTI lonafarnib improved platelet count and showed clin. response with limited efficacy and was associated with primarily diarrhea, gastrointestinal toxicity, anorexia and nausea in patient with MDS)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1290072 HCAPLUS
DOCUMENT NUMBER: 144:46998
TITLE: The X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compositions for antitumor drug design
INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005115454	A2	20051208	WO 2005-US15981	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

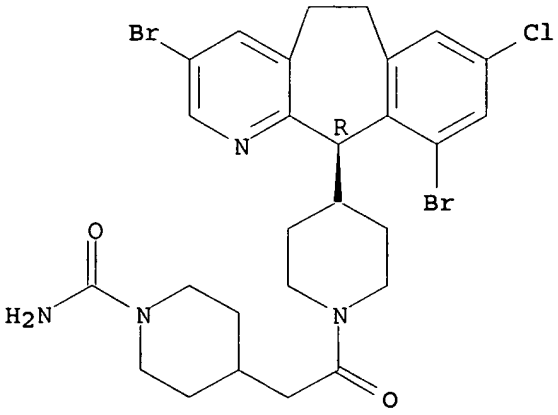
AB The present invention relates to compds. (e.g., peptidomimetics and non-peptides) that treat, prevent or stabilize cellular proliferative disorders and methods of treating, preventing, or stabilizing such disorders. The invention also provides three-dimensional structures of a BRCT domain-BACH1 phosphopeptide complex.

IT 193275-84-2, Sarasar
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compns. for antitumor drug design)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2005:1239173 HCAPLUS
DOCUMENT NUMBER:	143:477963
TITLE:	Preparation of pyrazolyl urea derivatives as TrkA kinase inhibitors useful in the treatment of cancer
INVENTOR(S):	Lee, Wendy; Ladouceur, Gaetan; Dumas, Jacques; Smith, Roger; Ying, Shihong; Wang, Gan; Chen, Zhi; Liu, Qingjie; Mokdad, Holia Hatoum
PATENT ASSIGNEE(S):	Bayer Pharmacueticals Corporation, USA
SOURCE:	PCT Int. Appl., 215 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110994	A2	20051124	WO 2005-US15106	20050502
WO 2005110994	A3	20060202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-566445P P 20040430
OTHER SOURCE(S): MARPAT 143:477963
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

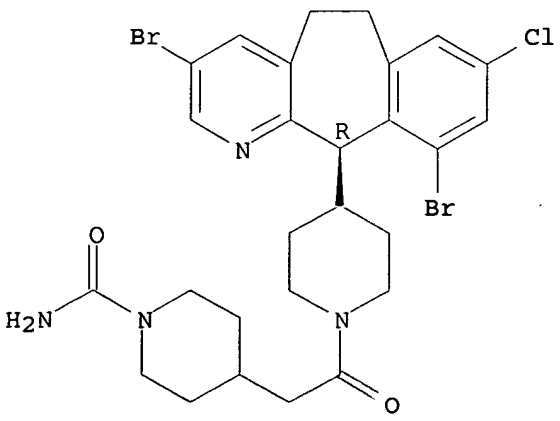
AB Title compds. I [R1-2 = H, alkyl, halo; A = Ph, pyridine, pyrimidine; B = phenylene, naphthylene; L = O, S, CH2; M = Ph, pyridine, pyrimidine; n = 0-1; X = O, SO2, etc.; Y = alkoxy, oxycarbonyl, amino, etc.] are prepared For instance, II is prepared from 4-[3-tert-butyl-5-[N'-[4-(pyridin-4-yloxy)phenyl]ureido]pyrazol-1-yl]benzoic acid Me ester (preparation given) and 2-(pyrrolidin-1-yl)ethylamine (DCE, AlMe3, 80°, 16 h). Compds. of the invention show significant inhibition of TrkA kinase (IC50 < 1 μM). I are useful for the treatment of cancer.

IT 193275-84-2, Lonafarnib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted pyrazolylurea derivs. useful for cancer treatment)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

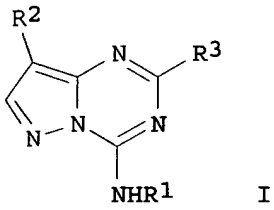


L12 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:904338 HCAPLUS
DOCUMENT NUMBER: 143:248417
TITLE: Preparation of pyrazolotriazines as kinase inhibitors for treating cancer and other diseases associated with a kinase
INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187219	A1	20050825	US 2005-64044	20050223
US 7038045	B2	20060502		
WO 2005082908	A1	20050909	WO 2005-US5614	20050223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006122389	A1	20060608	US 2006-335383	20060119

PRIORITY APPLN. INFO.: US 2004-547685P P 20040225
US 2005-64044 A3 20050223

OTHER SOURCE(S): MARPAT 143:248417
GI



I

AB In its many embodiments, the present invention provides a novel class of pyrazolo[1,5-a]triazine compds. (I, variables defined below) as inhibitors of kinases such as, for example, cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the kinases using such compds. or pharmaceutical compns. For I, R1 is H, optionally substituted alkyl, aryl, heteroaryl, heteroarylalkyl, arylalkyl, NR6R7, cycloalkyl and cycloalkylalkyl; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, trifluoromethyl, OR7, SR7, hydroxyalkyl, haloalkyl, aryl, heteroaryl, halo, CN, formyl, nitro, alkylcarbonyl, aralkylcarbonyl,

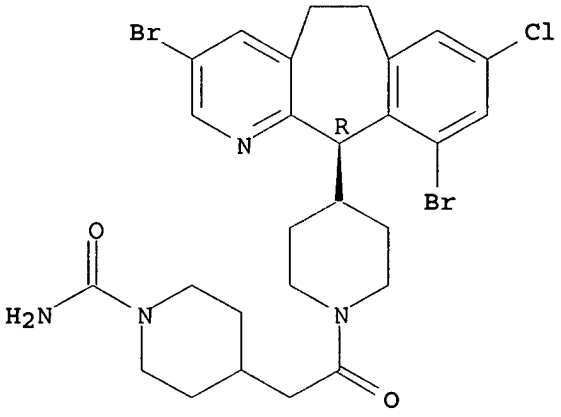
heteroaralkylcarbonyl, or alkylene-N(R8R9) [where R8 and R9 represent H or alkyl, or R8 and R9 taken together with the nitrogen in -N(R8R9) form a five- to seven-membered heterocycle]; R3 is -NR4R5, substituted heterocycle, H, alkyl, alkylthio, aralkylthio, alkylsulfinyl, or aralkylsulfinyl; R4 is optionally substituted alkyl, cycloalkyl or heterocyclyl; R5 is H, alkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, heterocyclyl, acyl or heteroarylalkyl; R6 is H, alkyl or aryl; R7 is H or alkyl.

IT 193275-84-2, SCH66336
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyrazolotriazines as kinase inhibitors for treating cancer and other diseases associated with kinase in combination with other anticancer agents)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:700420 HCAPLUS

DOCUMENT NUMBER: 143:259750

TITLE: Characterization of a human carcinoma cell line selected for resistance to the farnesyl transferase inhibitor 4-(2-(4-(8-chloro-3,10-dibromo-6,11-dihydro-5H-benzo-(5,6)-cyclohepta(1,2-b)-pyridin-11(R)-yl)-1-piperidinyl)-2-oxo-ethyl)-1-piperidinecarboxamide (SCH66336)

AUTHOR(S): Bruzek, Laura M.; Poynter, Jenny N.; Kaufmann, Scott H.; Adjei, Alex A.

CORPORATE SOURCE: Department of Oncology, Mayo Clinic, Rochester, MN, USA

SOURCE: Molecular Pharmacology (2005), 68(2), 477-486
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Farnesyl protein transferase inhibitors (FTIs) have demonstrated clin. activity in certain solid tumors and hematol. malignancies. Little is known about mechanisms of resistance to these agents. To provide a basis for better understanding FTI resistance,

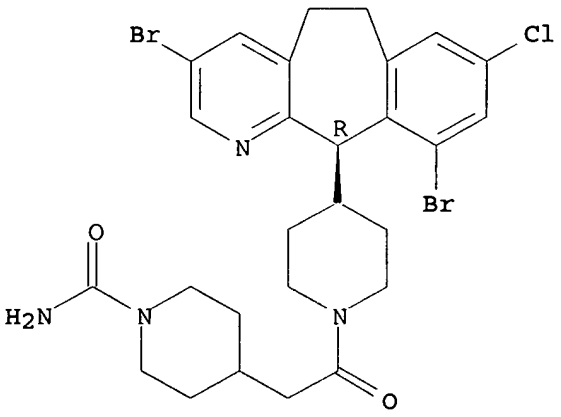
the colorectal carcinoma cell line HCT 116 was selected by stepwise exposure to increasing 4-(2-(4-(8-chloro-3,10-dibromo-6,11-dihydro-5H-benzo-(5,6)-cyclohepta(1,2-b)-pyridin-11(R)-yl)-1-piperidinyl)-2-oxo-ethyl)-1-piperidinecarboxamide (SCH66336) concns. The resulting line, HCT 116R, was 100-fold resistant to SCH66336 and other FTIs, including Me {N-[2-phenyl-4-N[2(R)-amino-3-mercaptopropylamino] benzoyl]}-methionate (FTI-277), but was less than 2-fold resistant to the standard agents gemcitabine, cisplatin, and paclitaxel. Accumulation of the unfarnesylated forms of prelamin A and HDJ-2, two substrates that reflect farnesyl transferase inhibition, was similar in FTI-treated parental and HCT 116R cells, indicating that alterations in drug uptake or inhibition of farnesyl protein transferase is not the mechanism of resistance. Changes in signal-transduction pathways that might account for this resistance were examined by immunoblotting and confirmed pharmacol. There was no difference in activation of the mitogen-activated protein kinase kinase (MEK)/extracellular signal-regulated kinase pathway or sensitivity to the MEK1/2 inhibitor 2'-amino-3'-methoxyflavone (PD98059) in HCT 116R cells. In contrast, increased phosphorylation of the mol. target of rapamycin (mTOR) and its downstream target p70 S6 kinase and increased levels of Akt1 and Akt2 were demonstrated in HCT 116R cells. Further expts. demonstrated that the mTOR inhibitor rapamycin selectively sensitized HCT 116R cells to SCH66336 but not to gemcitabine, cisplatin, or paclitaxel. These findings provide evidence that alterations in the phosphatidylinositol-3 kinase/Akt pathway can contribute to FTI resistance and suggest a potential strategy for overcoming this resistance.

IT 193275-84-2, SCH66336
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of a human carcinoma cell line selected for resistance to the farnesyl transferase inhibitor SCH66336)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:588556 HCAPLUS
DOCUMENT NUMBER: 143:115395
TITLE: Preparation of derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Jiang, Songchun; Zhang, Han-Zhong

PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005060663	A2	20050707	WO 2004-US42292	20041217
WO 2005060663	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-530256P P 20031218
GI

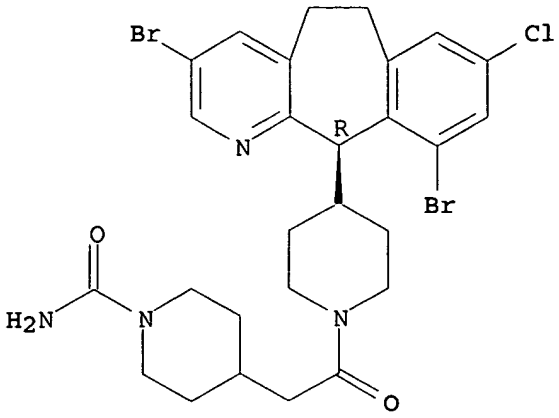
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to novel derivs. of gambogic acid (I) and analogs thereof. Thus, 2-(Dimethylamino)ethyl gambogate (II) was prepared from I via esterification with ClCH2CH2NMe2·HCl in the presence of KI and Cs2CO4. The present invention also relates to the discovery that novel derivs. of gambogic acid are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The bioactivity of II was determined [caspase cascade activation EC50 = 676 nM vs. T-47D and EC50 = 1041 nM vs. DLD breast cancer cells; cell proliferation inhibition GI50 = 187 nM (vs. T-47D), GI50 = 173 nM (vs. DLD), GI50 = 101 nM (vs. MX-1), GI50 = 180 nM (vs. SW620), GI50 = 184 nM (vs. H1299), GI50 = 440 nM (vs. HEK293T), GI50 = 192 nM (vs. HEK293H)].

IT 193275-84-2, SCH66336
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination chemotherapy co-agent; preparation of derivs. of gambogic acid and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409543 HCAPLUS
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148535	A1	20050707	US 2004-975974	20041028
CA 2542904	AA	20050512	CA 2004-2542904	20041029
EP 1682565	A1	20060726	EP 2004-789809	20041029
R: DE, FR, GB				

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030
WO 2004-CA1902 W 20041029

AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short

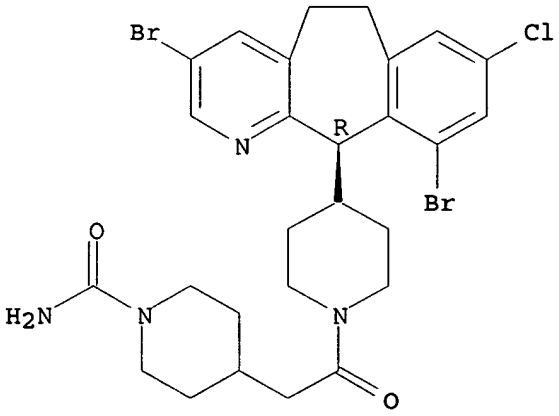
hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

IT 193275-84-2, Lonafarnib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409357 HCAPLUS
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

US 2005119217	A1	20050602	US 2004-975790	20041028
AU 2004284855	A1	20050512	AU 2004-284855	20041029
CA 2542884	AA	20050512	CA 2004-2542884	20041029
EP 1691842	A1	20060823	EP 2004-789807	20041029

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-516263P P 20031030
WO 2004-CA1900 W 20041029

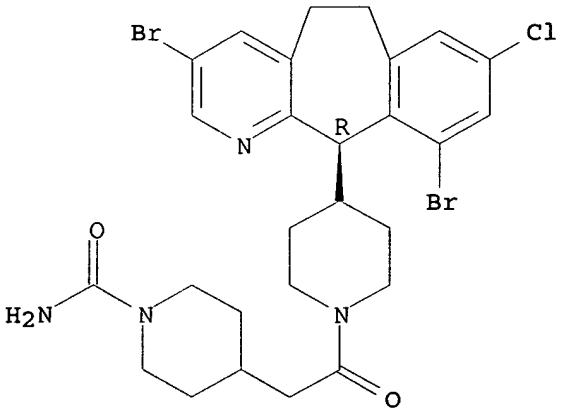
AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

IT 193275-84-2, Lonafarnib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with chemotherapeutic agent)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409226 HCAPLUS
DOCUMENT NUMBER: 142:441858
TITLE: Methods of using vitamin D compounds in the treatment of myelodysplastic syndromes
INVENTOR(S): Whitehouse, Martha J.; Curd, John G.

PATENT ASSIGNEE(S): Novacea, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 703,140, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

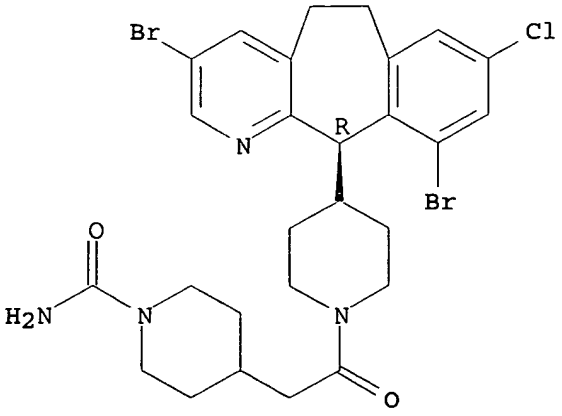
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005101576	A1	20050512	US 2004-841820	20040510
PRIORITY APPLN. INFO.:			US 2003-703140 B2	20031106

AB Methods of treating MDS, or ameliorating a symptom thereof, are disclosed. Specific methods encompass the administration of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Other methods include intermittent administration of a high dose of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Such intermittent administration allows high doses of the vitamin D compds. to be administered while minimizing or eliminating hypercalcemia. Patients having low risk MDS and refractory anemia unresponsive to erythropoietin were entered into a Phase 2 trial to evaluate the effect of high dose pulse administration of calcitriol. Patients were administered weekly oral calcitriol at a dose of 45 μg for 20 consecutive weeks. The calcitriol was formulated in a composition containing the following excipients with the amount given in approx. percentage by weight: 65 % MIGLYol 812N, 30 % GELUCIRE 44/14, 5 % vitamin-E TPGS and about 0.05 % each of butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA). The high dose pulse administration of calcitriol showed beneficial effect for the treatment of MDS.

IT 193275-84-2, SARASAR
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

RN 193275-84-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

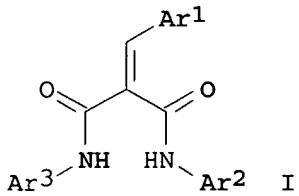


L12 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:369221 HCAPLUS
DOCUMENT NUMBER: 142:430024
TITLE: Preparation of substituted 2-arylmethylene-N-aryl-N'-aryl-malonamides and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Pervin, Azra; Kasibhatla, Shailaja; Nguyen, Bao Ngoc
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037196	A2	20050428	WO 2004-US32570	20041005
WO 2005037196	A3	20051013		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-508290P P 20031006
OTHER SOURCE(S): MARPAT 142:430024
GI



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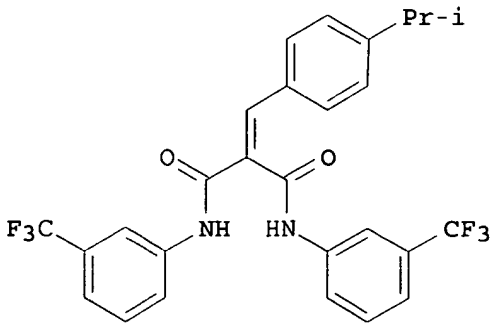


II

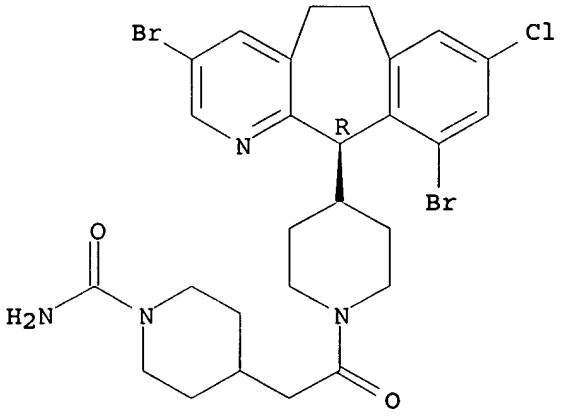
AB Substituted 2-arylmethylene-N-aryl-N'-aryl-malonamides and analogs I [wherein Ar1, Ar2, Ar3 = independently (un)substituted hetero/aryl, hetero/arylalkyl, (partially) saturated carbocyclic, heterocyclic] were prepared as activators of caspases and inducers of apoptosis for treating neoplasm. For example, II was prepared by acylation of with 3-aminobenzotrifluoride malonyl dichloride and reaction of the diamide with 4-isopropylbenzaldehyde. II exhibited caspase activation (EC50 = 15 nM for human breast cancer cell line T-47D), inhibition of cell proliferation (GI50 = 180 nM for T-47D). II induced apoptosis in Jurkat and T-47D cells. I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

IT 193275-84-2, SCH 66336
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of 2-arylmethylene-N,N'-diarylmalonamides and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283298 HCAPLUS
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

AU 2004273910	A1	20050331	AU 2004-273910		20040916
CA 2538570	AA	20050331	CA 2004-2538570		20040916
EP 1670477	A2	20060621	EP 2004-788798		20040916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
NO 2006001325	A	20060606	NO 2006-1325		20060323
PRIORITY APPLN. INFO.:			US 2003-504310P	P	20030918
			WO 2004-US30368	W	20040916

OTHER SOURCE(S): MARPAT 142:349042

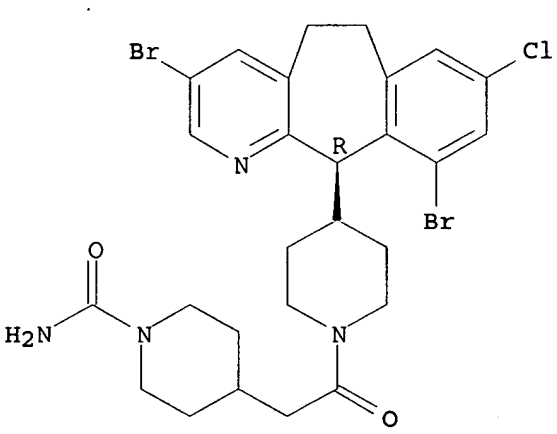
AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT 193275-84-2, Lonafarnib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorpromazine compound-antiproliferative drug antitumor combination)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2005:63766 HCAPLUS
DOCUMENT NUMBER:	143:53006
TITLE:	Hyperleukocytosis complicating lonafarnib treatment in patients with chronic myelomonocytic leukemia
AUTHOR(S):	Buresh, A.; Perentesis, J.; Rimsza, L.; Kurtin, S.; Heaton, R.; Sugrue, M.; List, A.
CORPORATE SOURCE:	Departments of Medicine and Pathology, The Arizona Cancer Center, University of Arizona College of Medicine, Tucson, AZ, USA
SOURCE:	Leukemia (2005), 19(2), 308-310 CODEN: LEUKED; ISSN: 0887-6924
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal
LANGUAGE:	English

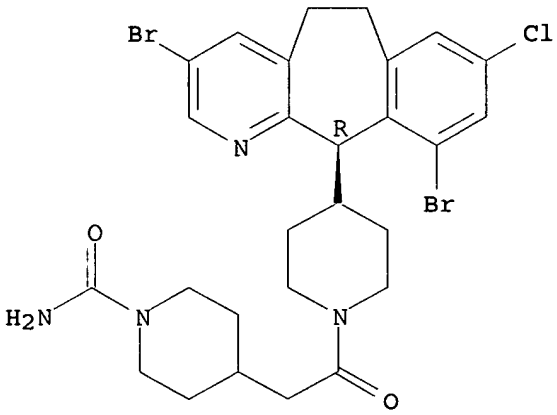
AB Lonafarnib is a member of a novel class of therapeutics under investigation in hematol. malignancies, termed the farnesyl transferase inhibitors (FTIs). Three patients with chronic myelomonocytic leukemia (CMML) who developed lonafarnib-associated hyperleukocytosis are described. In two cases, lonafarnib treatment was also associated with respiratory distress that resolved promptly following treatment with dexamethasone or study drug withdrawal. An infectious etiol. was excluded in both patients presenting with pulmonary infiltrates, whereas cytol. examination of the bronchioalveolar lavage fluid in the other patient confirmed alveolar infiltration by mature monocytes. Despite associated neutrophilia, expansion of a comparatively mature monocytic clone distinguishes these cases from the leukemia differentiation syndrome described with all-trans-retinoic acid treatment of acute promyelocytic leukemia. These cases represent the first description of leukemia differentiation-like syndrome occurring in patients treated with an FTI. Patients with proliferative CMML (white blood cell count above 12,000/μl) in particular appear to be at significant risk for this complication.

IT 193275-84-2, Lonafarnib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl transferase inhibitor lonafarnib caused hyperleukocytosis and pulmonary sequestration syndrome in chronic myelomonocytic leukemia human)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:895355 HCAPLUS
DOCUMENT NUMBER: 142:211151
TITLE: Clinical Activity of Farnesyl Transferase Inhibitors in Hematologic Malignancies: Possible Mechanisms of Action
AUTHOR(S): Jabbour, Elias; Kantarjian, Hagop; Cortes, Jorge
CORPORATE SOURCE: Department of Leukemia, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Leukemia & Lymphoma (2004), 45(11), 2187-2195
CODEN: LELYEA; ISSN: 1042-8194
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

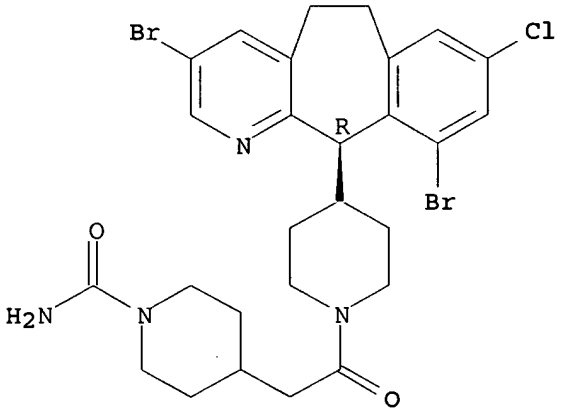
AB A review. Farnesyl transferase inhibitors (FTIs) are a novel class of anti-cancer agents that competitively inhibit farnesyl protein transferase (FTase). Initially developed to inhibit the prenylation necessary for Ras activation, their mechanism of action seems to be more complex, involving other proteins unrelated to Ras. FTIs have been developed and tested across a wide range of human cancers. At least 3 agents within this family have been investigated in hematol. malignancies . These are tipifarnib (R115777, Zarnestra), lonafarnib (SCH66336, SarasarTM), both of which are orally administered, and BMS-214662, which is given i.v. Preliminary results from clin. trials demonstrate enzyme target inhibition, a favorable toxicity profile and promising efficacy. Ongoing studies will better determine their mechanism of action and the role of combination with other agents, defining their place in the therapeutic arsenal of hematol. disorders.

IT 193275-84-2, Sarasar
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. trials with farnesyl transferase inhibitor lonafarnib demonstrated enzyme target inhibition, favorable toxicity profile and promising efficacy in hematol. malignancies)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:756710 HCAPLUS

DOCUMENT NUMBER: 141:277628

TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.

INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301
WO 2004078747	C1	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235829	A1	20041125	US 2004-788029	20040227
AU 2004217977	A1	20040916	AU 2004-217977	20040301
CA 2517361	AA	20040916	CA 2004-2517361	20040301
US 2004229937	A1	20041118	US 2004-789446	20040301
US 2005032798	A1	20050210	US 2004-788405	20040301
US 2005038031	A1	20050217	US 2004-788426	20040301
EP 1599467	A1	20051130	EP 2004-716144	20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004007897	A	20060301	BR 2004-7897	20040301
JP 2006519264	T2	20060824	JP 2006-508977	20040301

PRIORITY APPLN. INFO.:	US 2003-450323P	P	20030228
	US 2003-450324P	P	20030228
	US 2003-450348P	P	20030228
	WO 2004-US6286	A	20040301

OTHER SOURCE(S): MARPAT 141:277628

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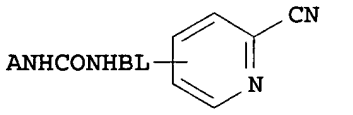

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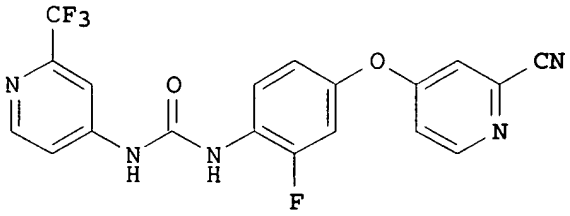


II

AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4-pyridylamine was stirred 20 h with carbonyldiimidazole in CH2Cl2; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC50 = 7.86 nM to >1600 nM.

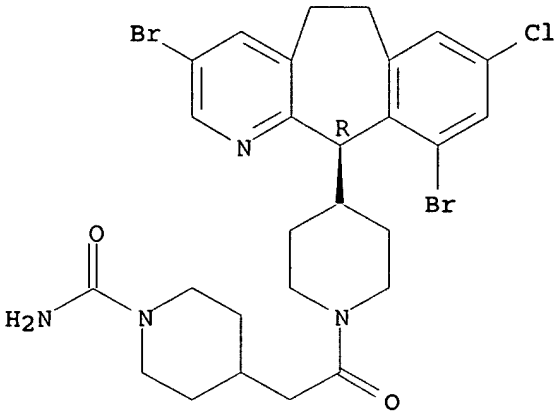
IT 193275-84-2, Lonafarnib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

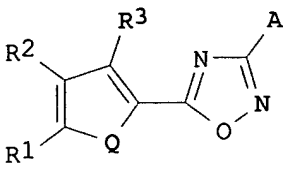
L12 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:565086 HCAPLUS
DOCUMENT NUMBER: 141:123632
TITLE: Preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Zhang, Han-zhong; Kuemmerle, Jared D.; Zhang, Hong; Kemnitzer, William E.
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058253	A1	20040715	WO 2003-US40308	20031218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004127521	A1	20040701	US 2003-737865	20031218
CA 2509224	AA	20040715	CA 2003-2509224	20031218
AU 2003303373	A1	20040722	AU 2003-303373	20031218
EP 1581213	A1	20051005	EP 2003-808469	20031218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1756547	A	20060405	CN 2003-80106440	20031218
JP 2006516250	T2	20060629	JP 2004-563731	20031218

PRIORITY APPLN. INFO.: US 2002-433953P P 20021218
WO 2003-US40308 W 20031218

OTHER SOURCE(S): MARPAT 141:123632

GI



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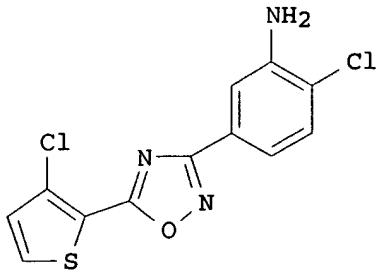


II

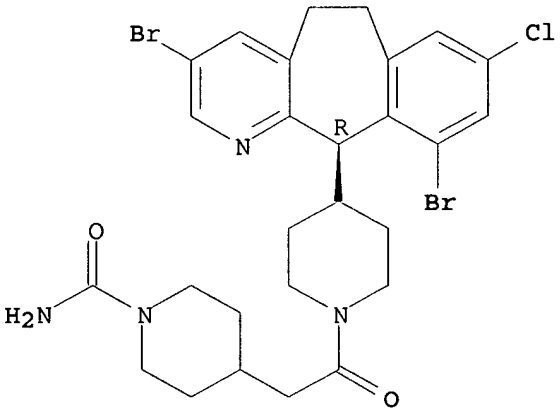
AB Title compds. I [R1-3 = H, halo, haloalkyl, aryl, etc.; Q = S, O, amino; A = heterocycle, carbocycle] are prepared For instance, 3-amino-4-chlorobenzamidoxime (preparation given) is reacted with 3-chlorothiophene-2-carbonyl chloride (pyridine, reflux, 50 min) to give II. II and other examples are potent caspase cascade activators and inducers of apoptosis in solid tumor cells, e.g., human breast cancer cell lines T-47D and ZR-75-1.

IT 193275-84-2, SCH66336
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:559502 HCAPLUS
DOCUMENT NUMBER: 141:190802
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors
INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-yu; James, Ray A.;

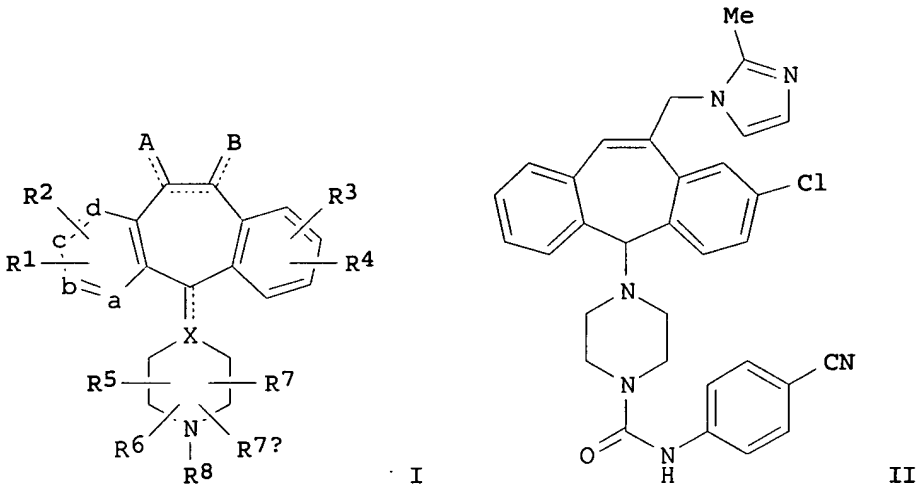
Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004122018	A1	20040624	US 2002-325896	20021219
US 2002198216	A1	20021226	US 2001-940811	20010828
US 2003229099	A1	20031211	US 2002-85896	20020227
US 2004122018	A1	20040624	US 2002-325896	20021219

PRIORITY APPLN. INFO.:

US 2001-940811	A2	20010828
US 2002-85896	A2	20020227
US 2002-325896	A	20021219
US 2000-229183P	P	20000830

GI



I II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention

inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

IT 740819-70-9P 740819-71-0P 740819-72-1P
740819-73-2P 740819-74-3P 740819-75-4P
740819-76-5P 740819-77-6P 740819-78-7P
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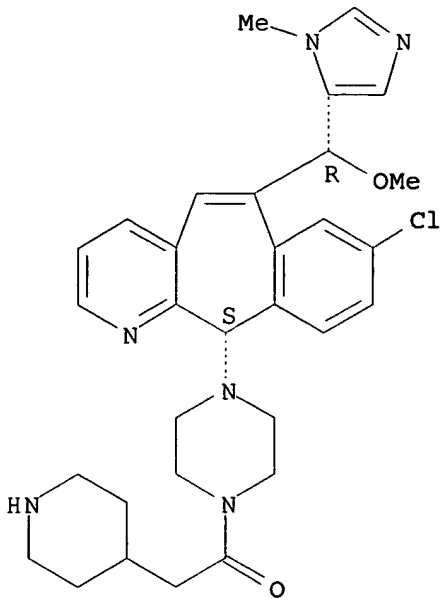
740822-34-8P 740822-35-9P 740822-36-0P
740822-37-1P 740822-38-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FPT inhibitor; preparation of tricyclic antitumor agents as farnesyl protein transferase inhibitors for treatment of cancer and other proliferative diseases)

RN 740819-70-9 HCAPLUS

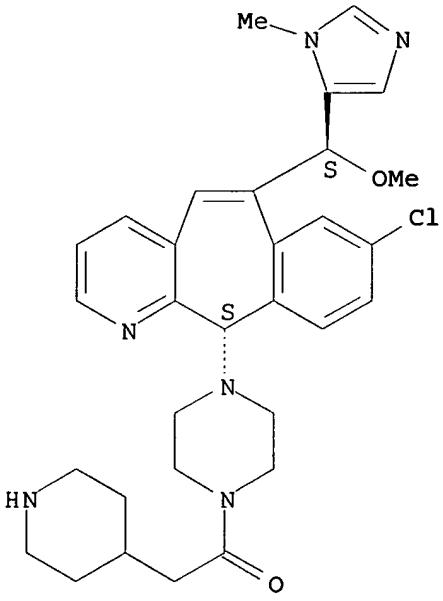
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



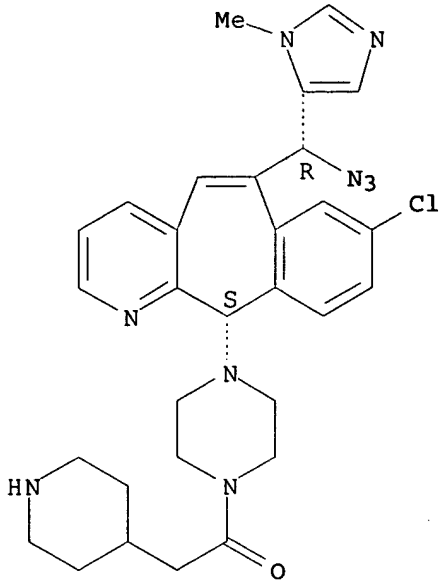
RN 740819-71-0 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



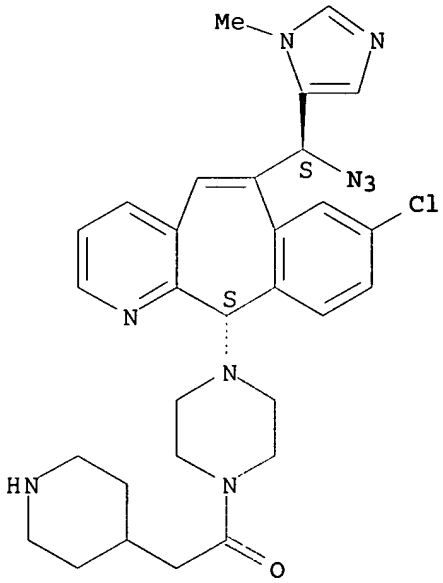
RN 740819-72-1 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



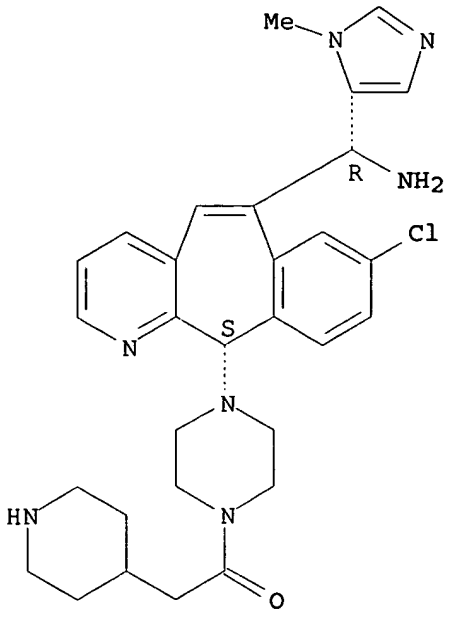
RN 740819-73-2 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



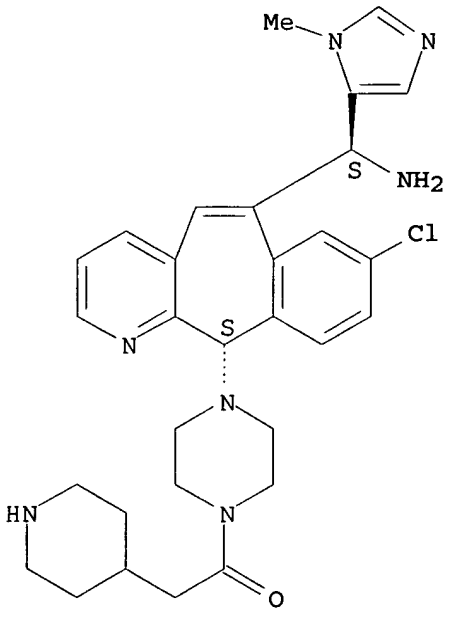
RN 740819-74-3 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



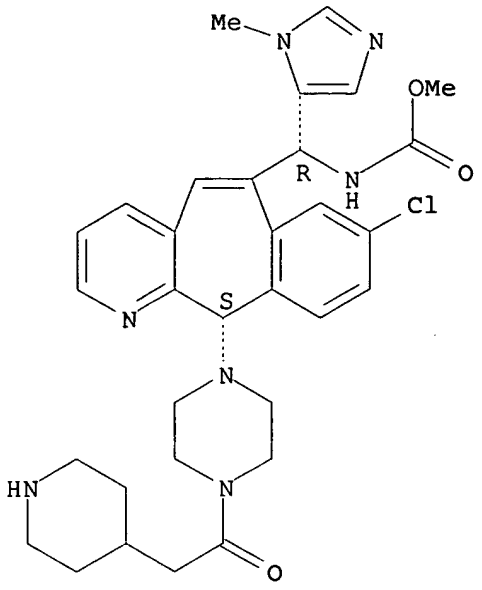
RN 740819-75-4 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



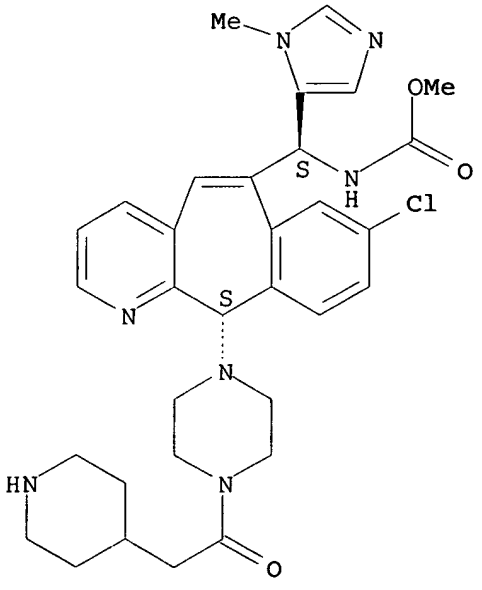
RN 740819-76-5 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



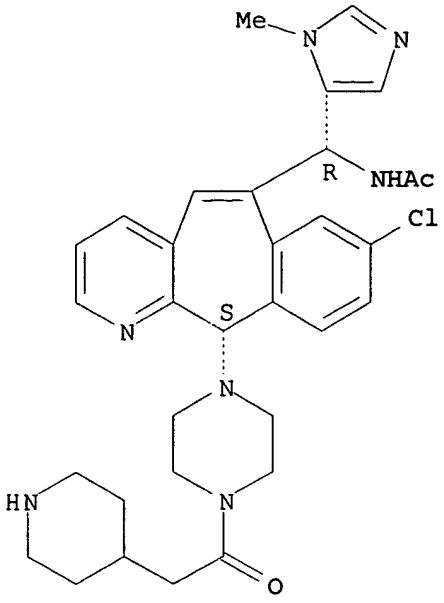
RN 740819-77-6 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



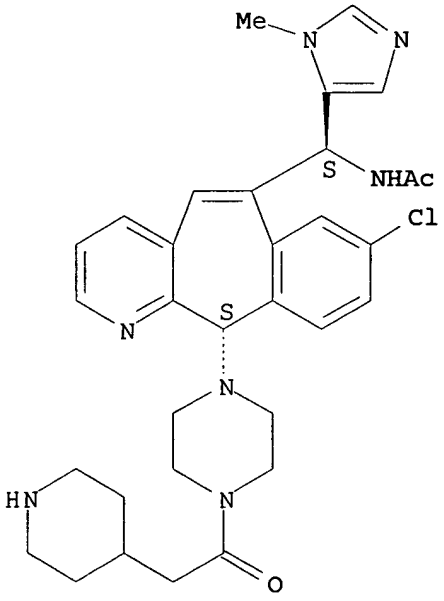
RN 740819-78-7 HCAPLUS
CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



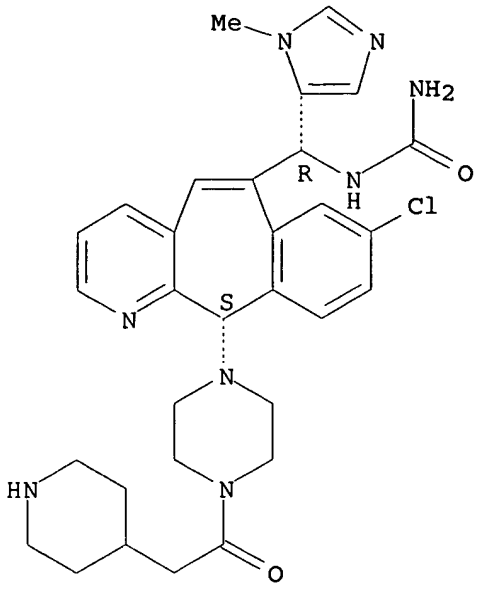
RN 740819-79-8 HCAPLUS
CN Acetamide, N-[(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



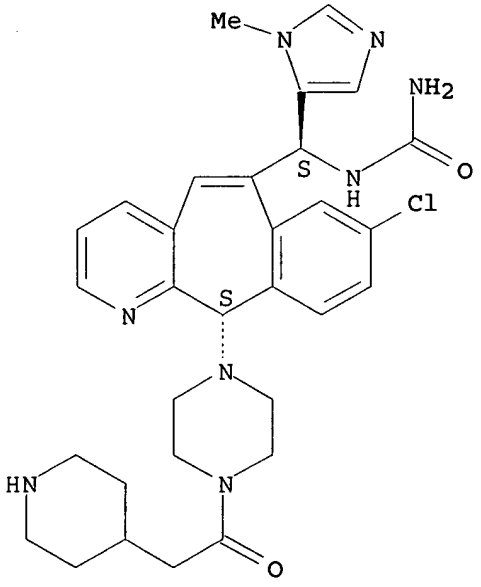
RN 740819-80-1 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



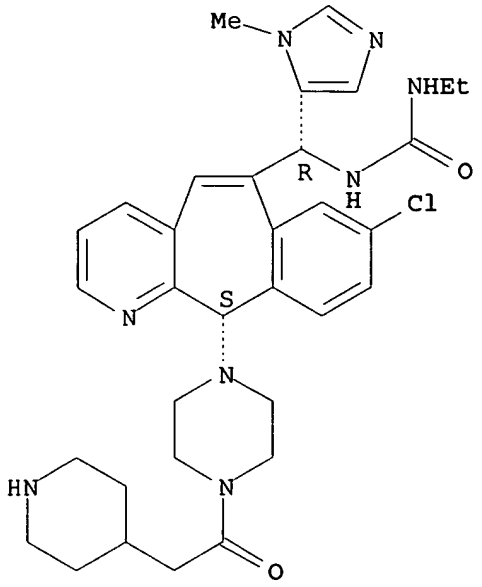
RN 740819-81-2 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



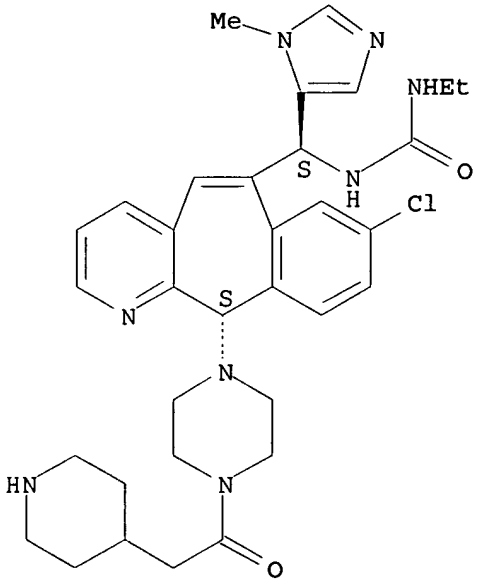
RN 740819-82-3 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



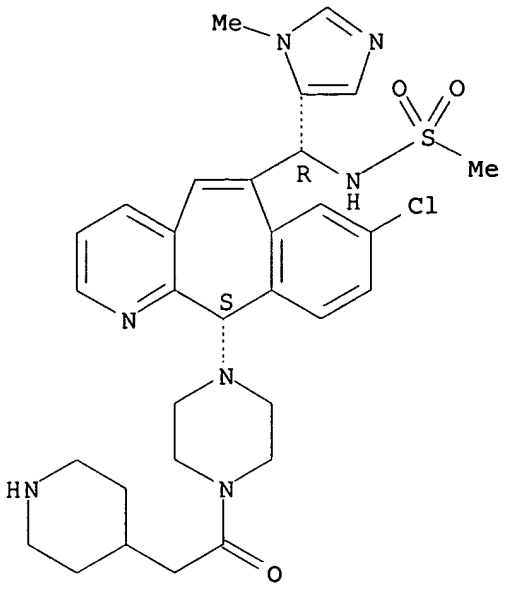
RN 740819-83-4 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



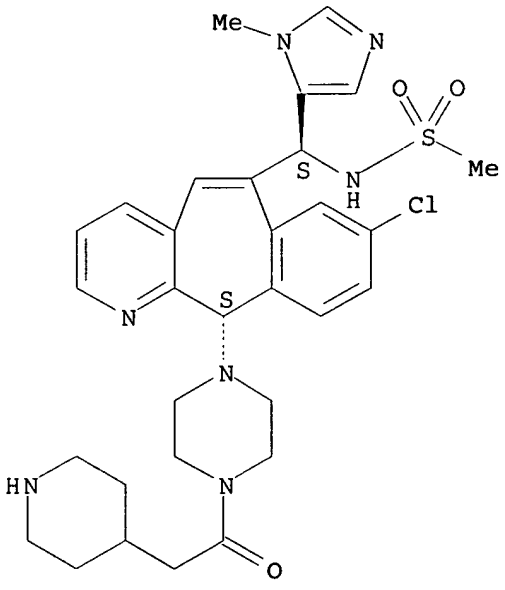
RN 740819-84-5 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



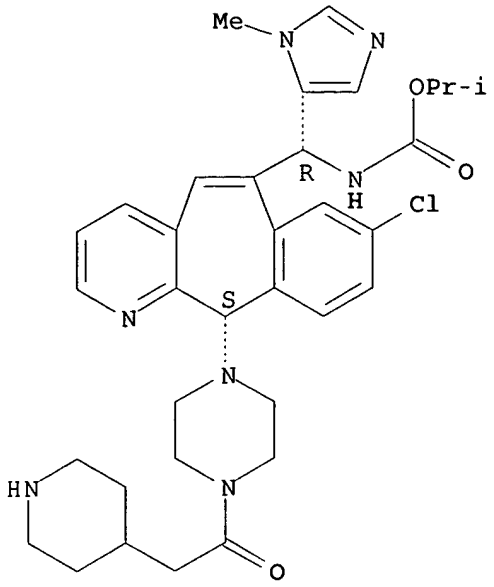
RN 740819-85-6 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



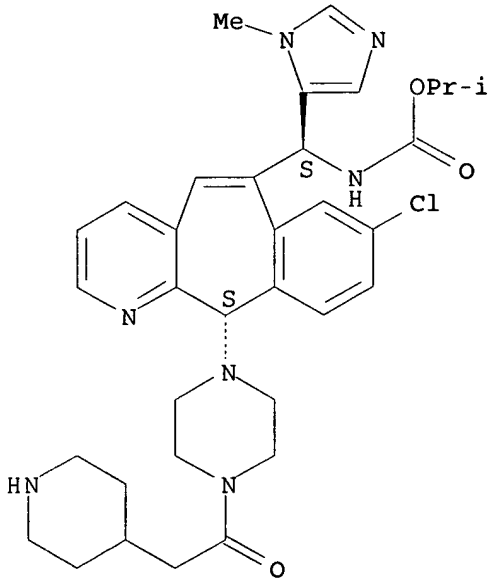
RN 740819-86-7 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



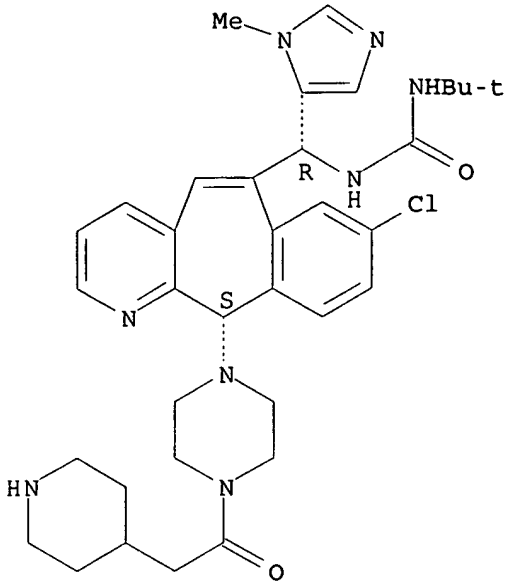
RN 740819-87-8 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



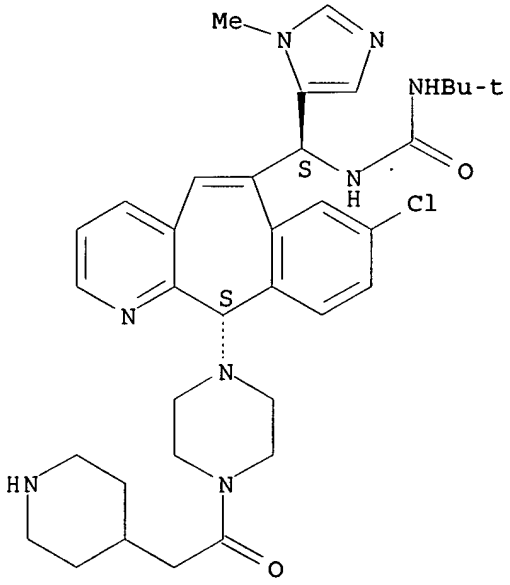
RN 740819-88-9 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



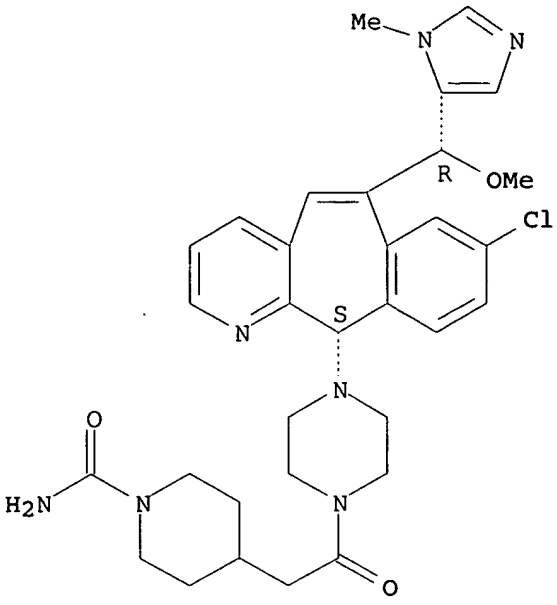
RN 740819-89-0 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



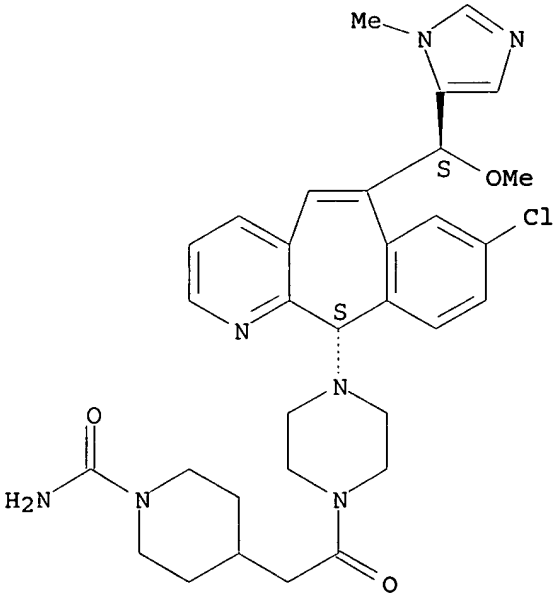
RN 740819-90-3 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



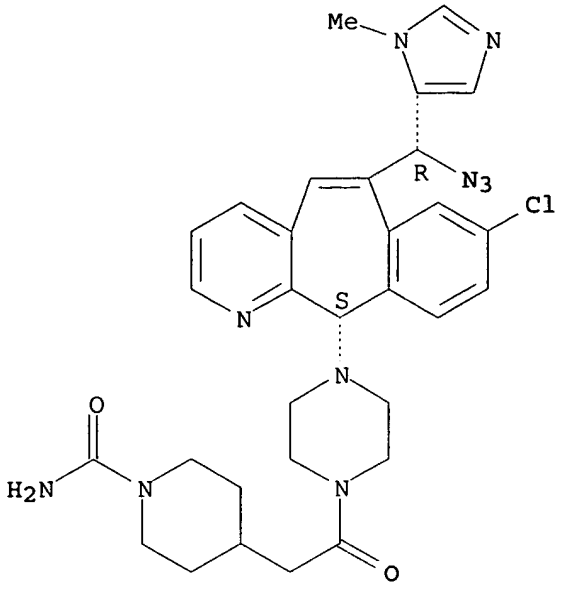
RN 740819-91-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



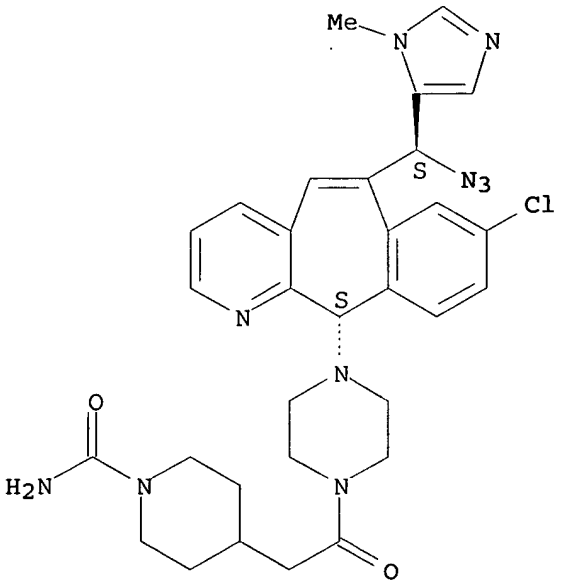
RN 740819-92-5 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



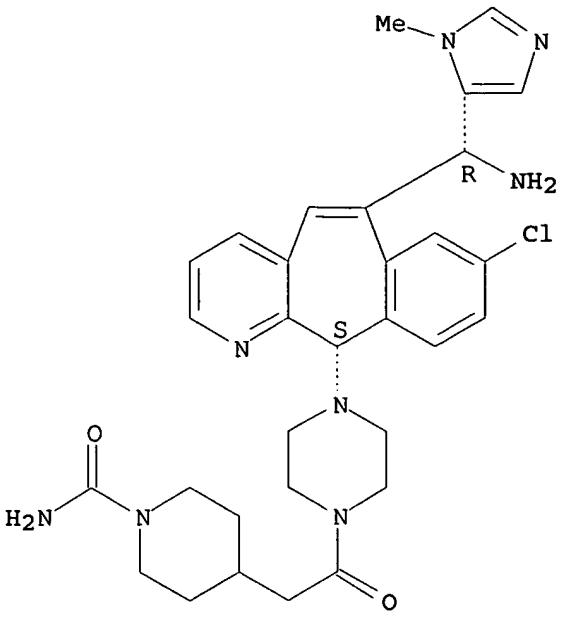
RN 740819-93-6 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



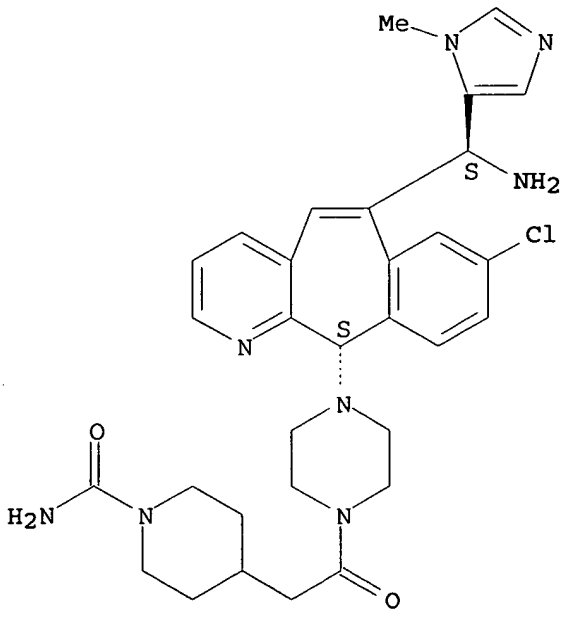
RN 740819-94-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



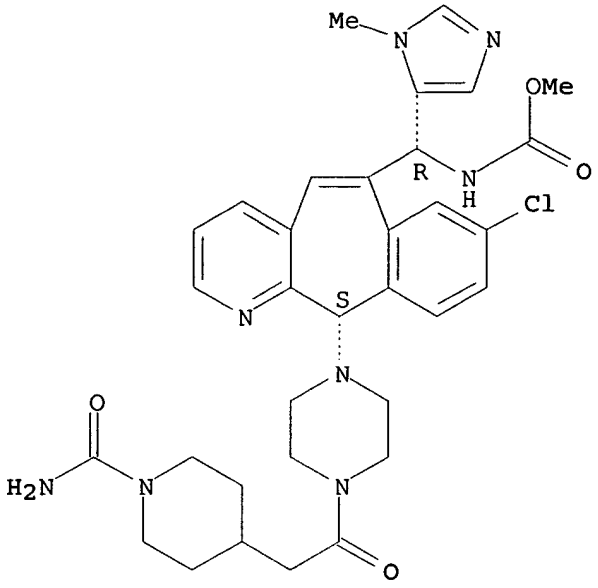
RN 740819-96-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



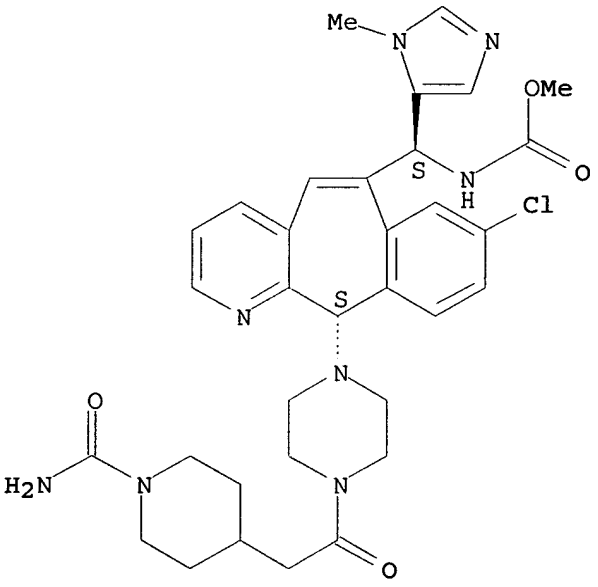
RN 740819-97-0 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



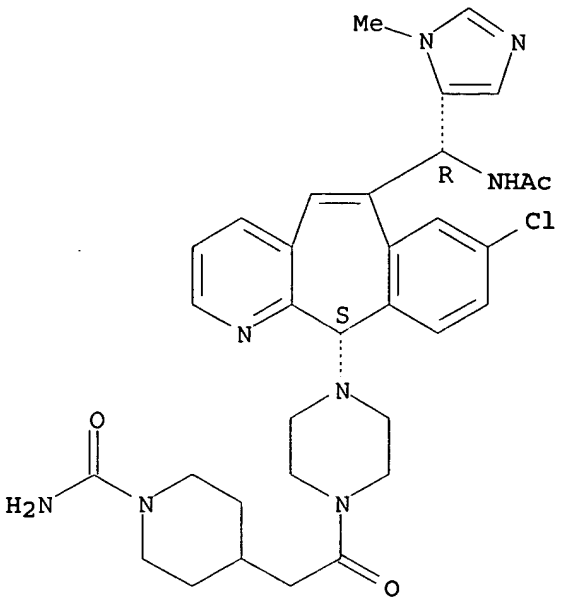
RN 740819-98-1 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



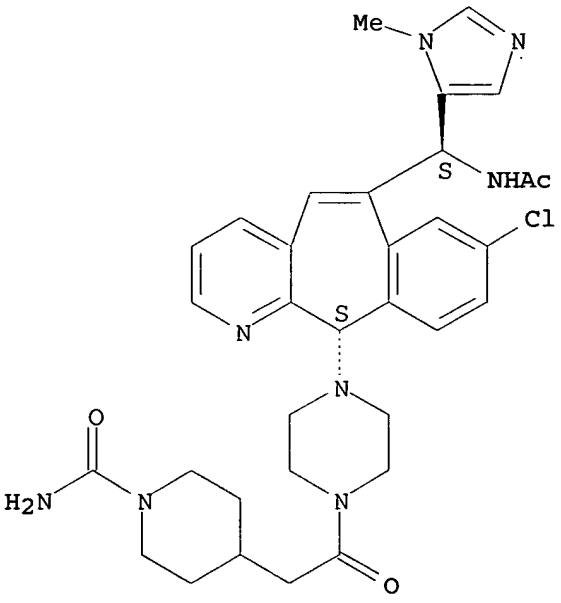
RN 740819-99-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-(acetylamino)(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



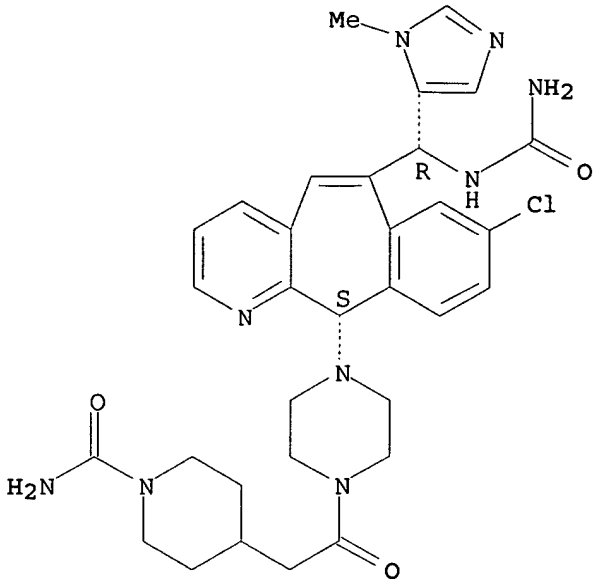
RN 740820-00-2 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-(acetylamino)(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



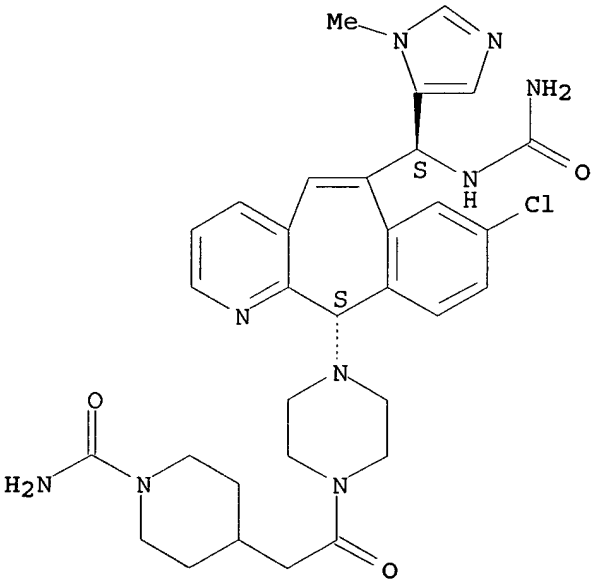
RN 740820-01-3 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



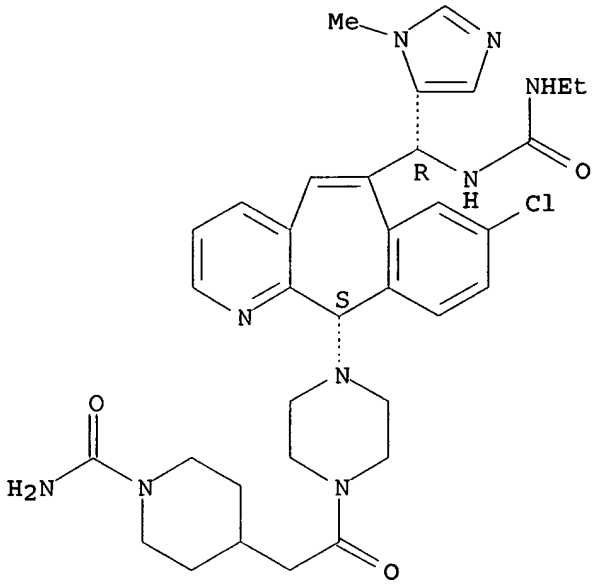
RN 740820-02-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



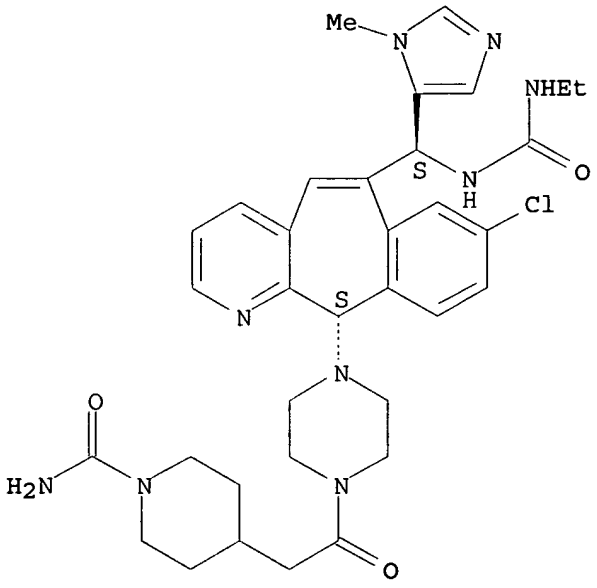
RN 740820-03-5 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



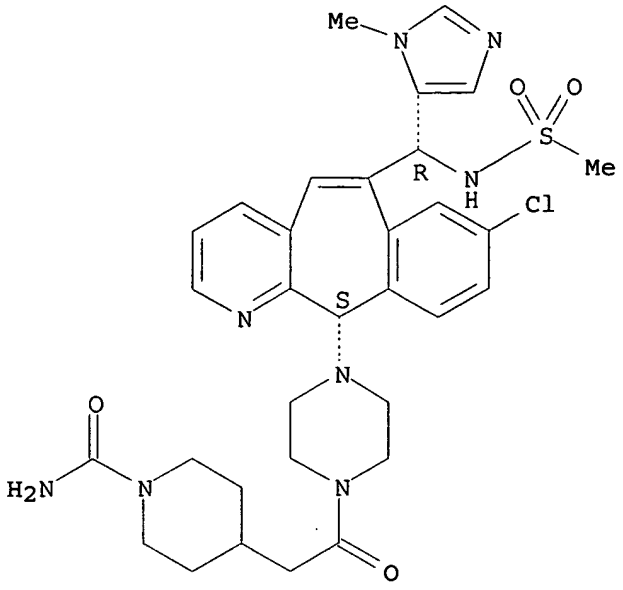
RN 740820-04-6 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



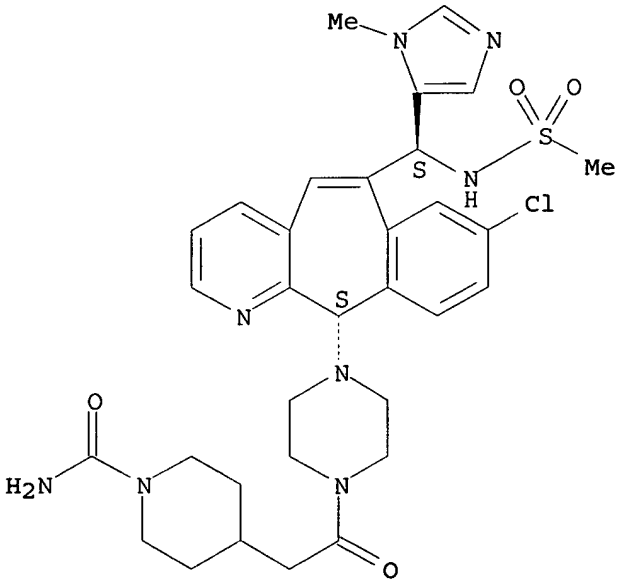
RN 740820-05-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



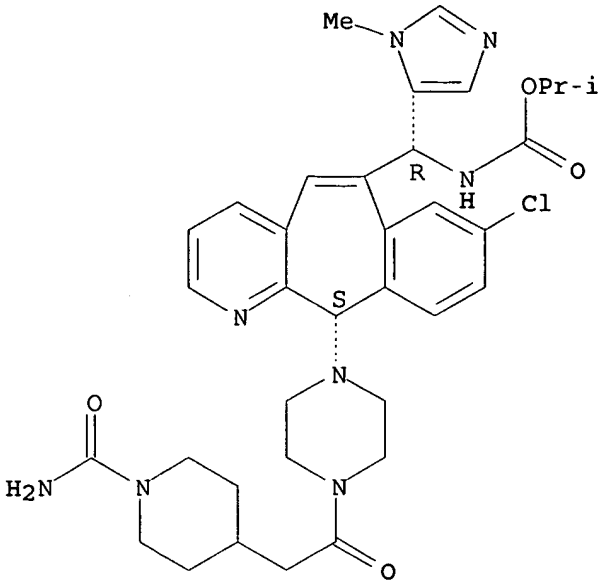
RN 740820-06-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



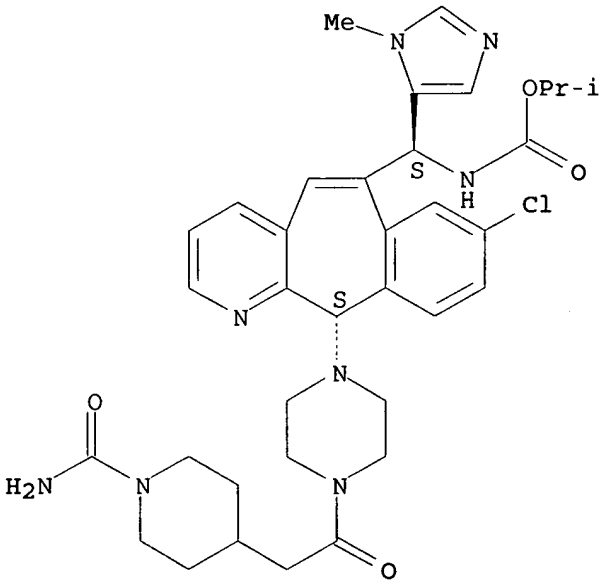
RN 740820-07-9 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



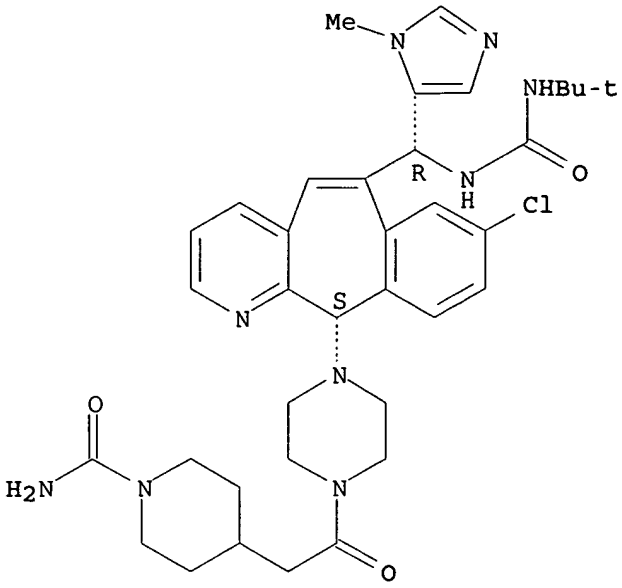
RN 740820-08-0 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



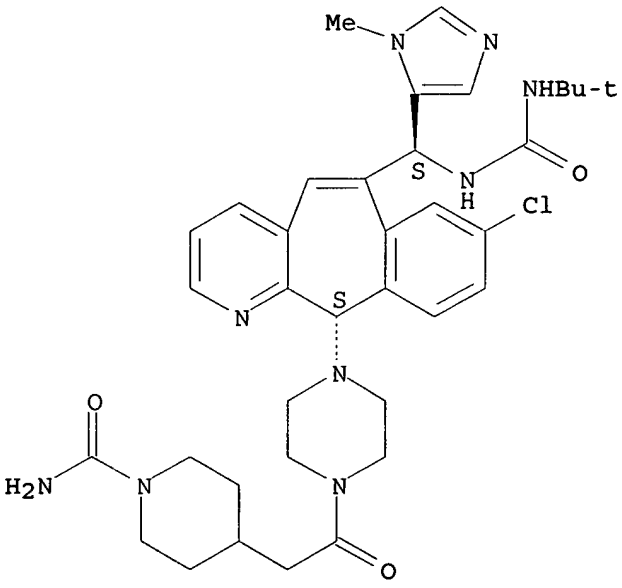
RN 740820-09-1 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



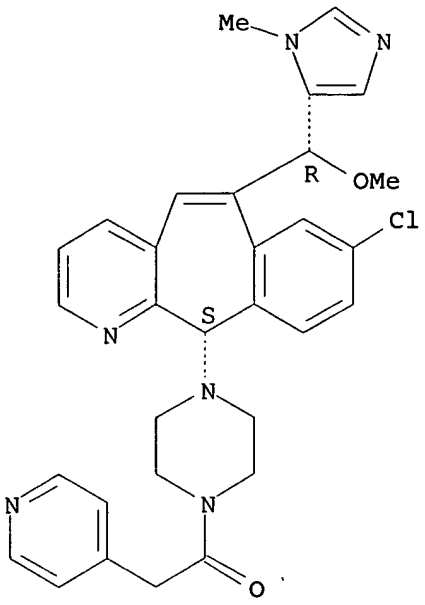
RN 740820-10-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



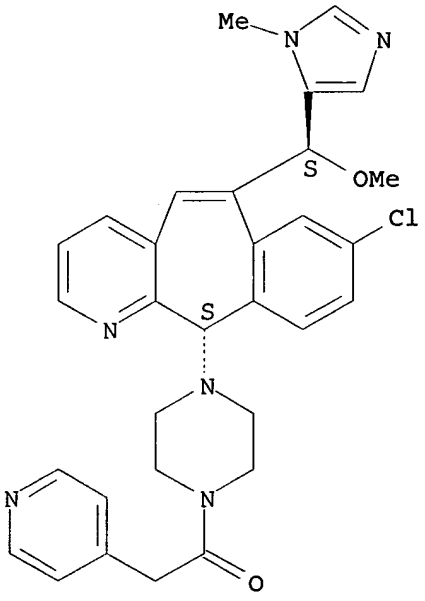
RN 740821-99-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



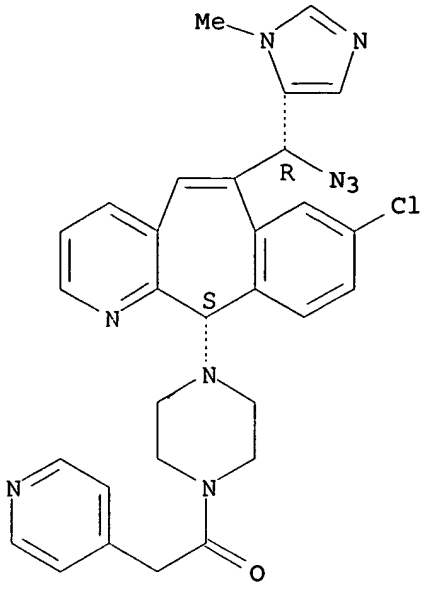
RN 740822-00-8 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



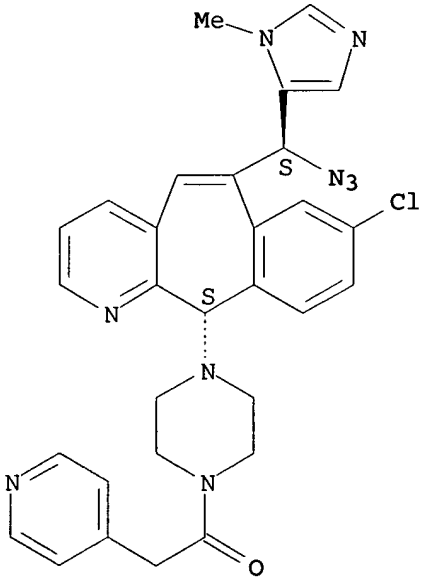
RN 740822-01-9 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



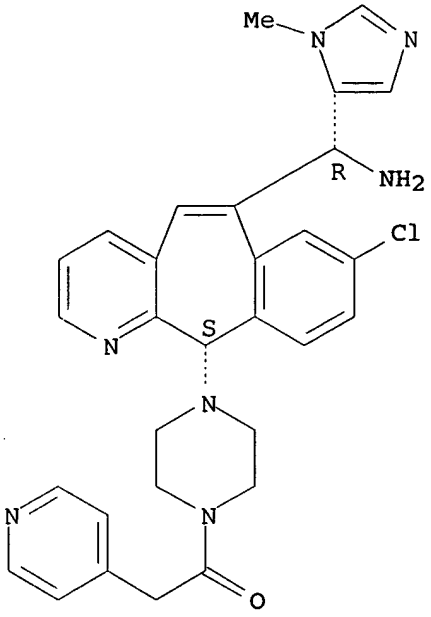
RN 740822-02-0 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



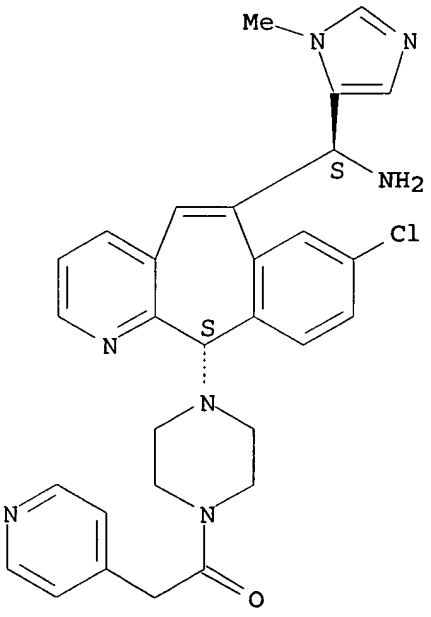
RN 740822-03-1 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



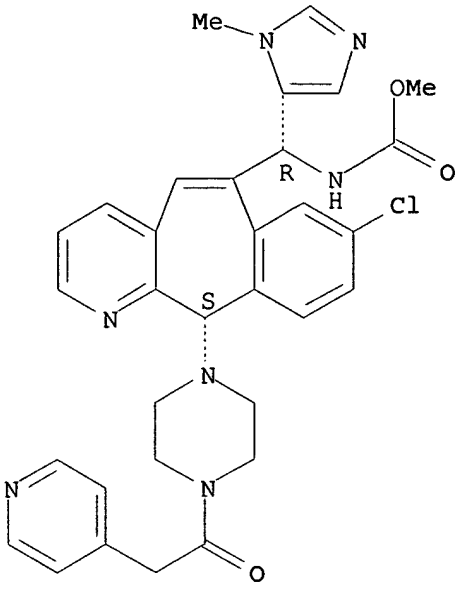
RN 740822-04-2 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



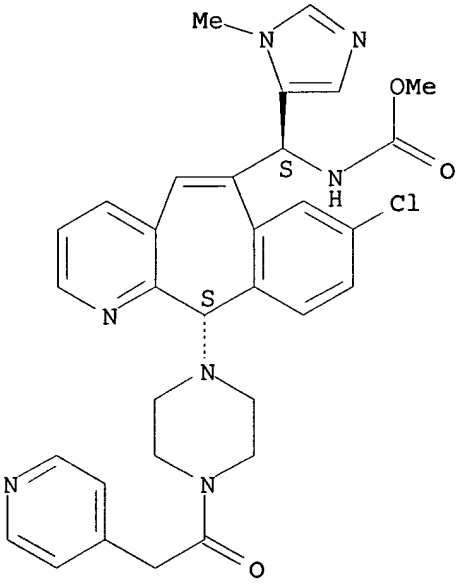
RN 740822-05-3 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



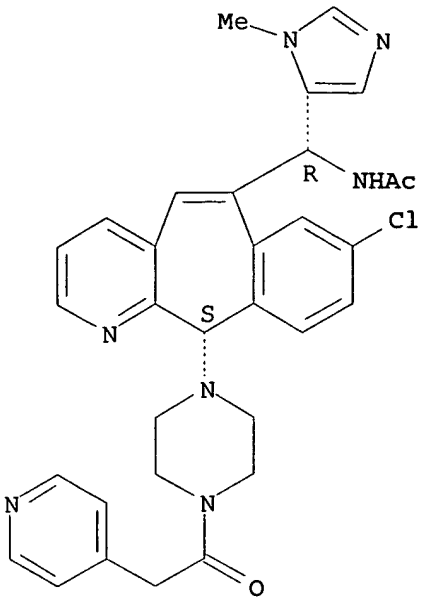
RN 740822-06-4 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



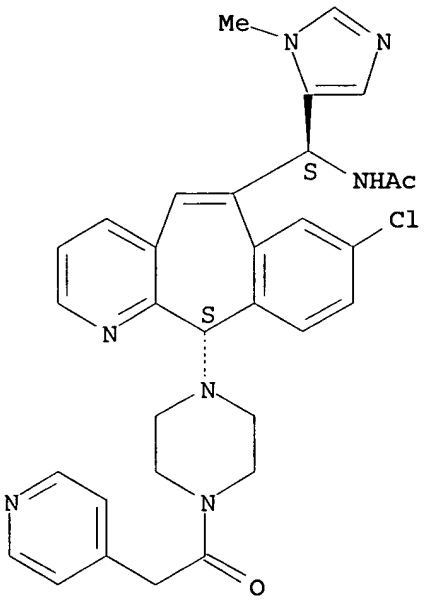
RN 740822-07-5 HCAPLUS
CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



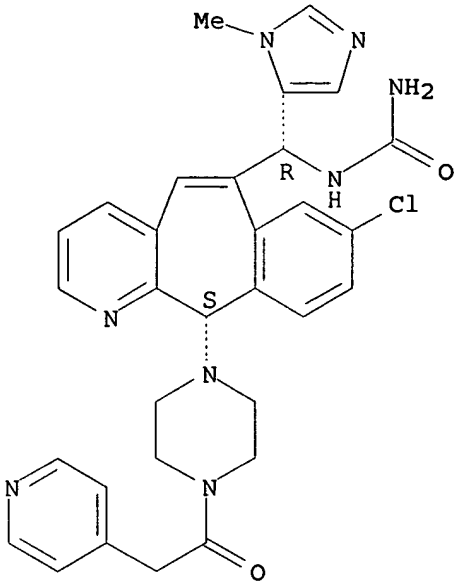
RN 740822-08-6 HCAPLUS
CN Acetamide, N-[(S)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



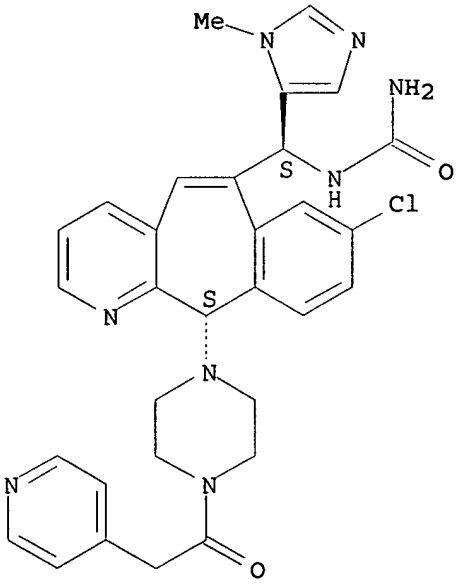
RN 740822-09-7 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



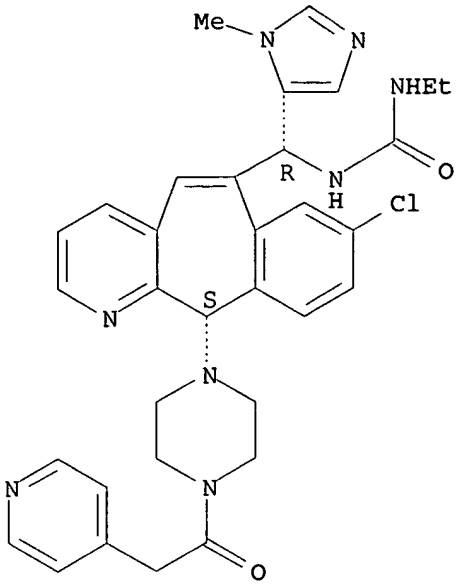
RN 740822-10-0 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



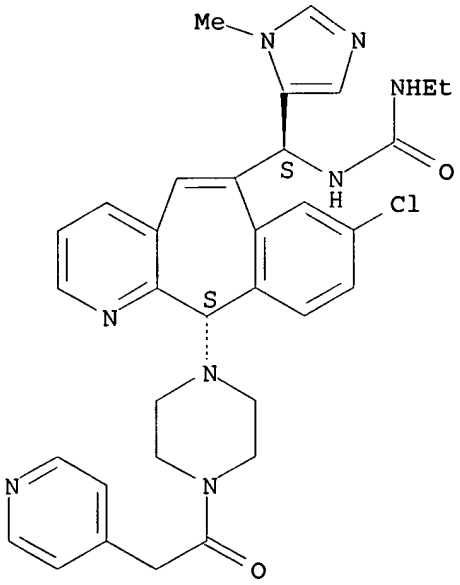
RN 740822-11-1 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



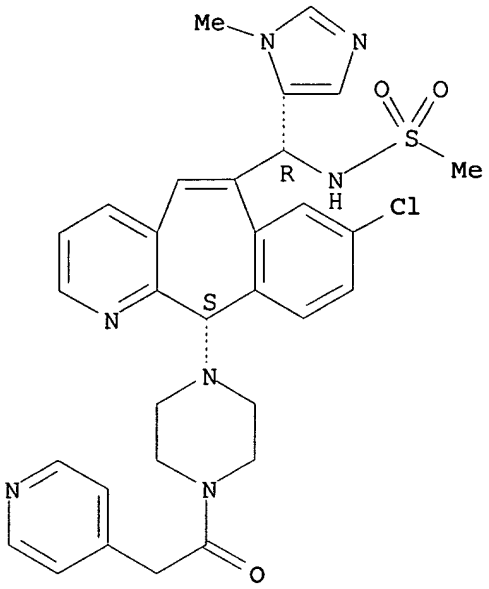
RN 740822-12-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



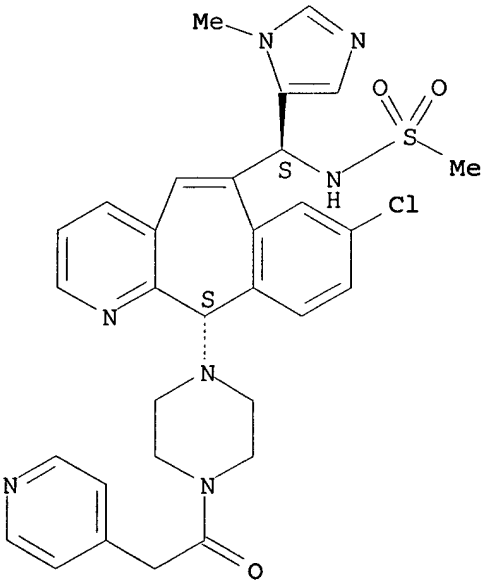
RN 740822-13-3 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



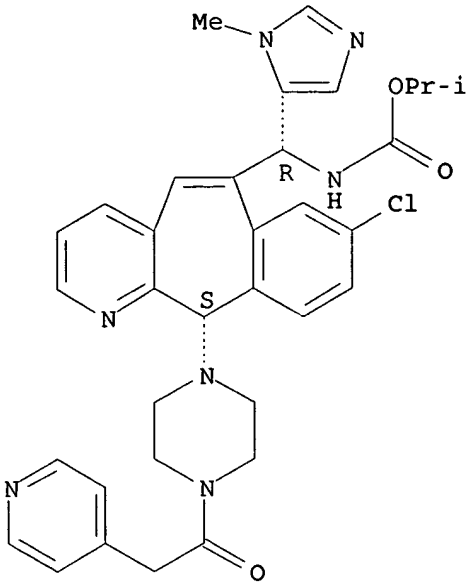
RN 740822-14-4 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



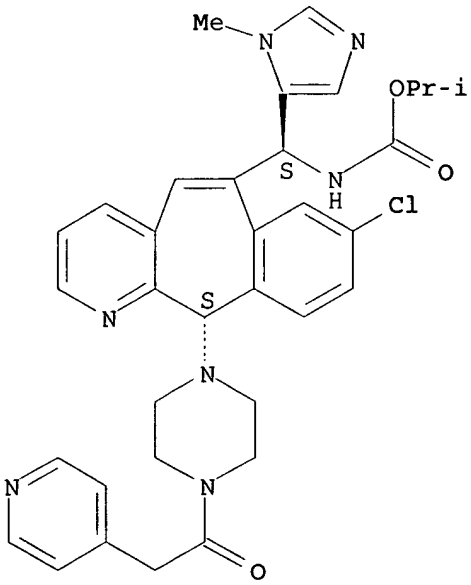
RN 740822-15-5 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



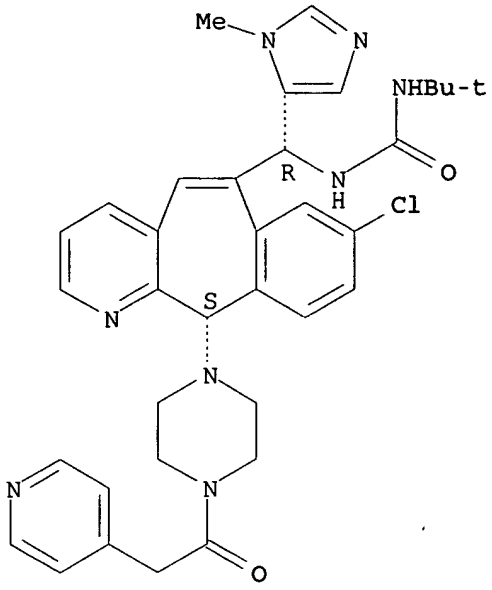
RN 740822-16-6 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



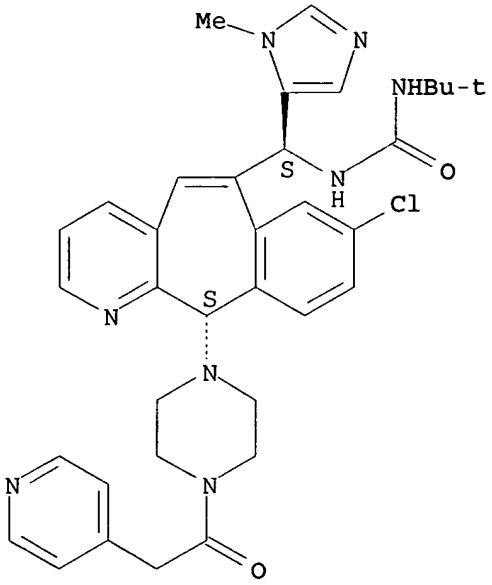
RN 740822-17-7 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



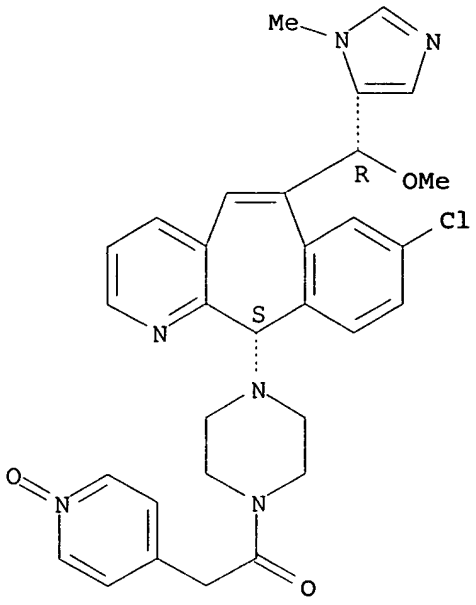
RN 740822-18-8 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



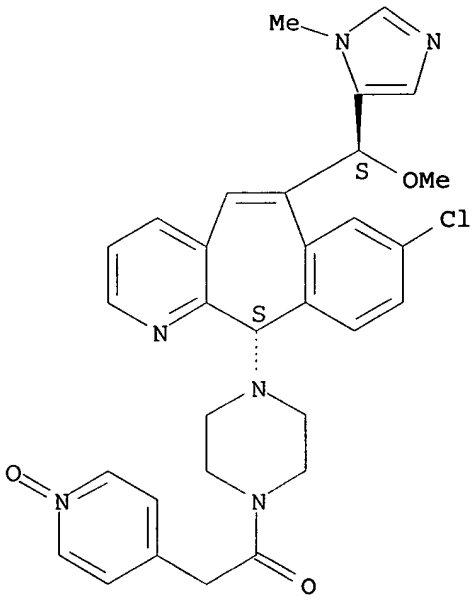
RN 740822-19-9 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



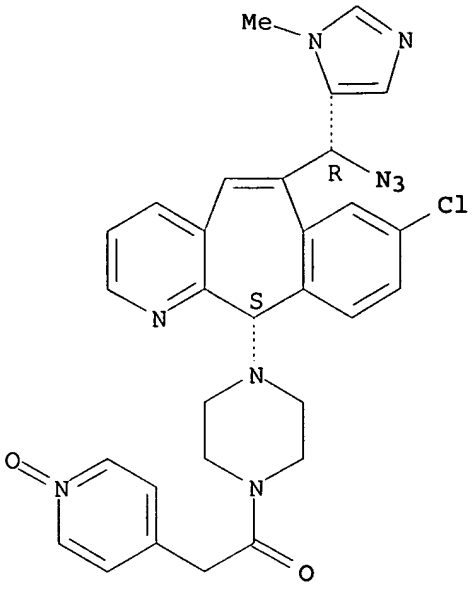
RN 740822-20-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



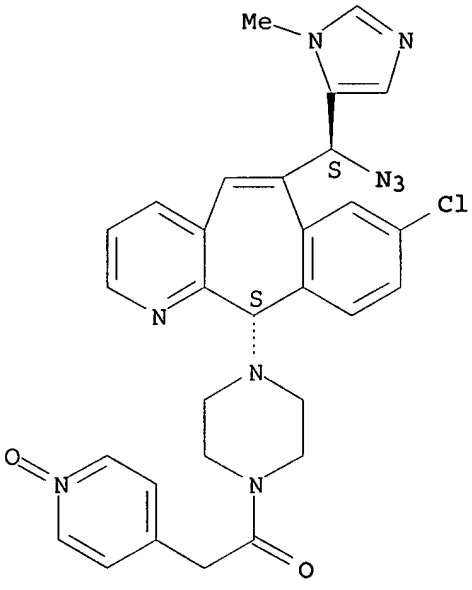
RN 740822-21-3 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



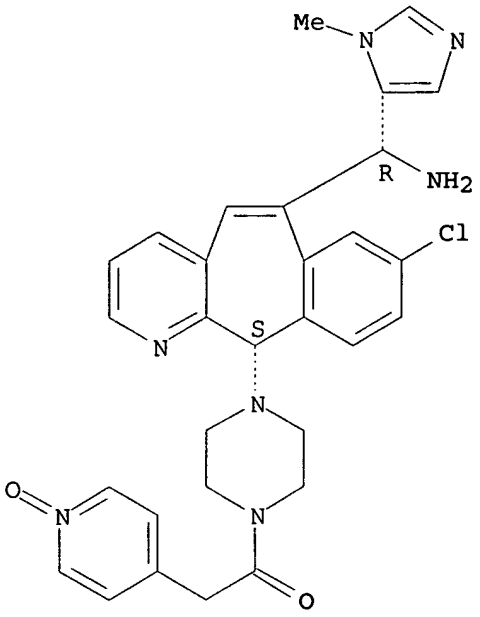
RN 740822-22-4 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



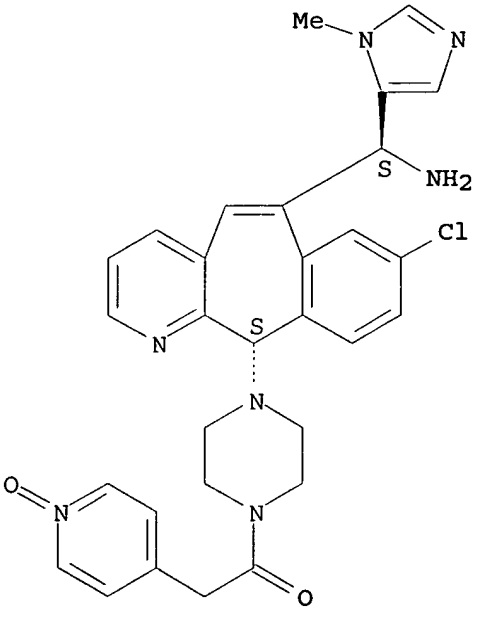
RN 740822-23-5 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



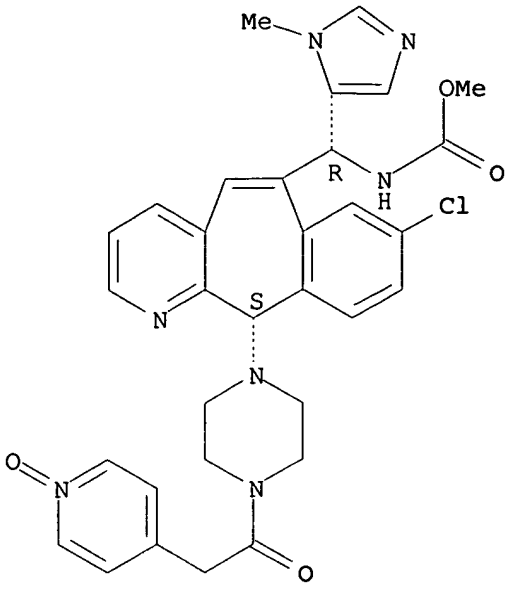
RN 740822-24-6 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



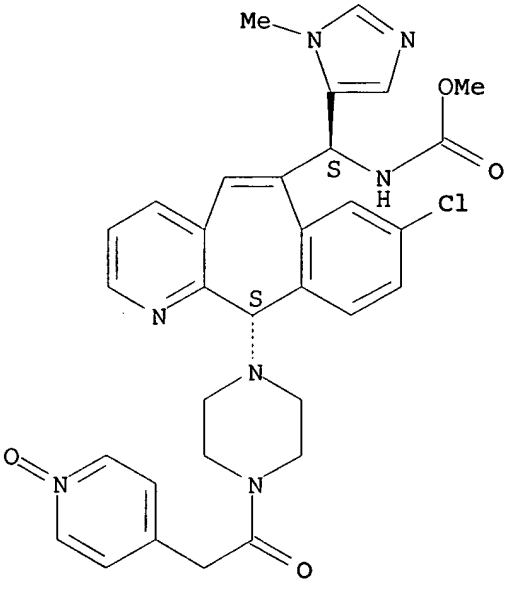
RN 740822-25-7 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



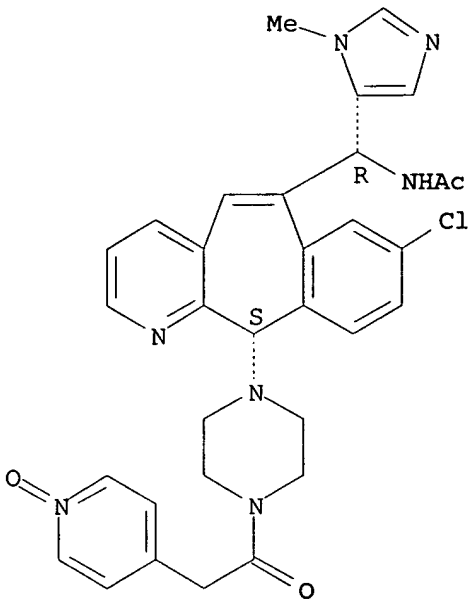
RN 740822-26-8 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



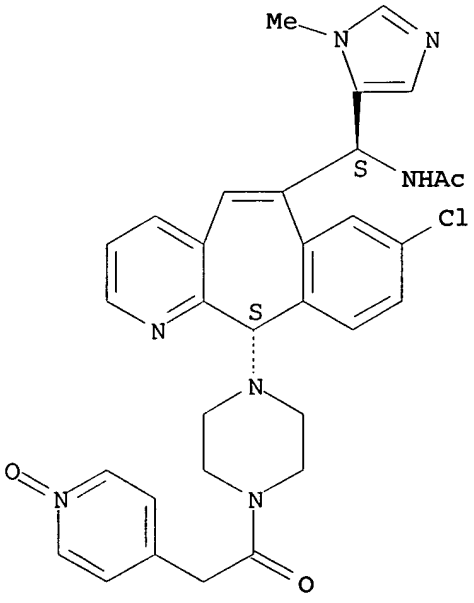
RN 740822-27-9 HCAPLUS
CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



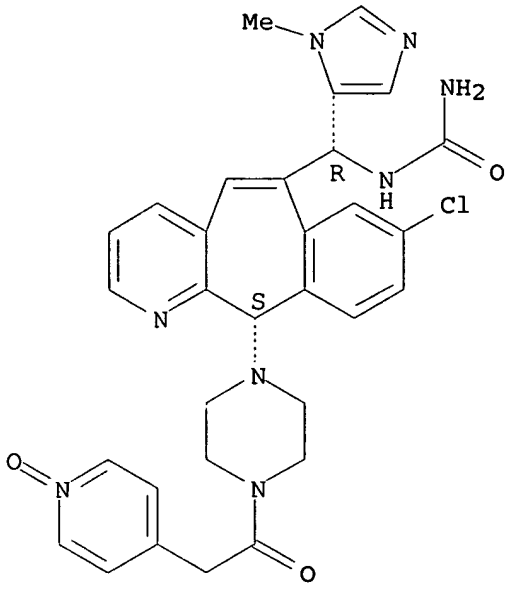
RN 740822-28-0 HCAPLUS
CN Acetamide, N-[(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



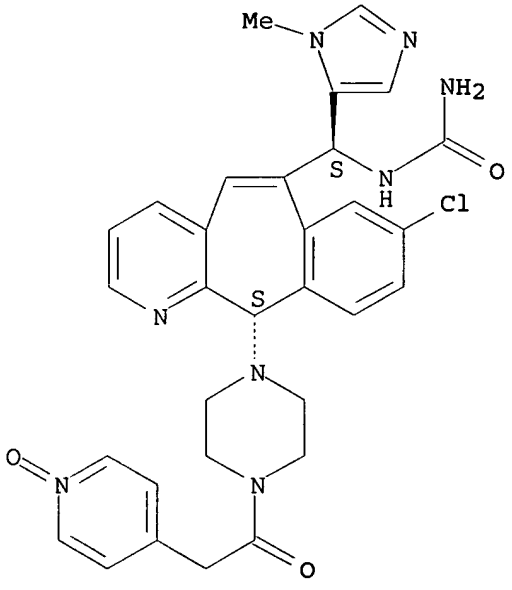
RN 740822-29-1 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



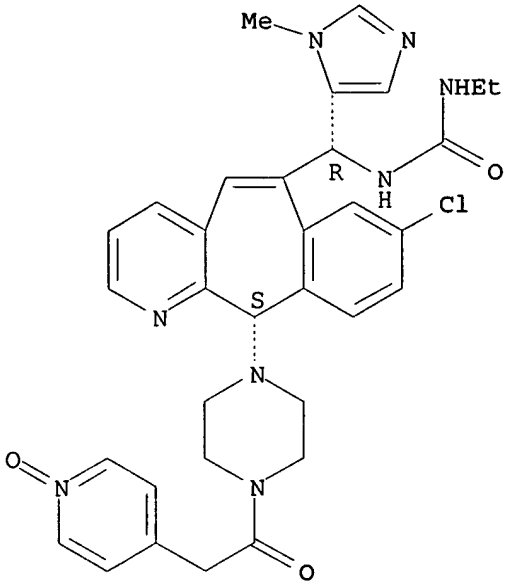
RN 740822-30-4 HCAPLUS
CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



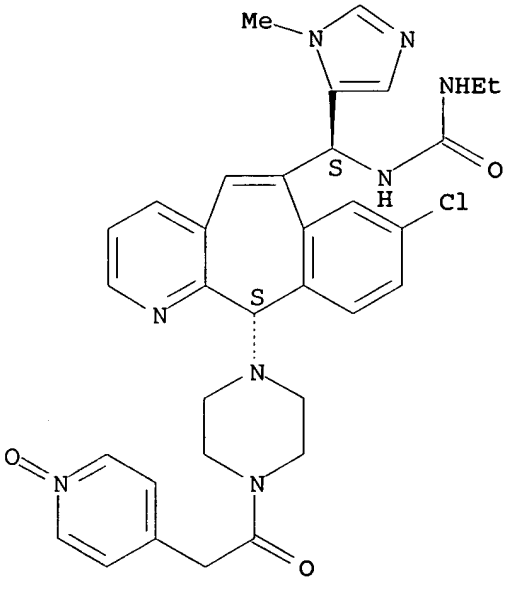
RN 740822-31-5 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



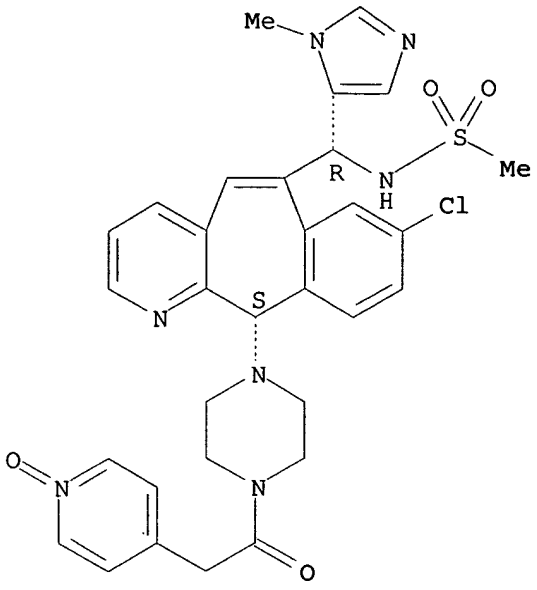
RN 740822-32-6 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



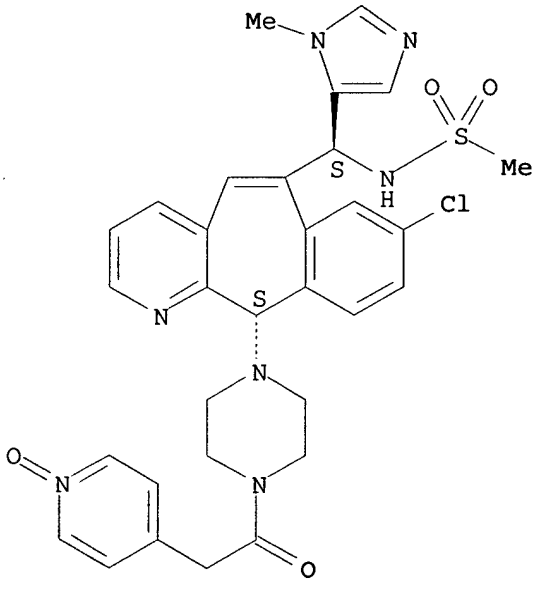
RN 740822-33-7 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



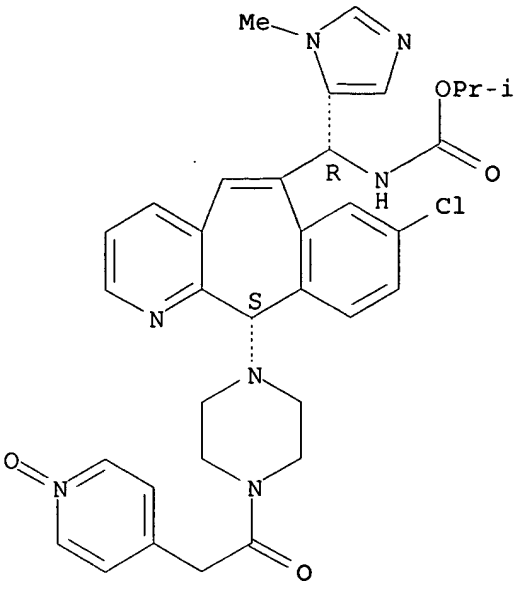
RN 740822-34-8 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



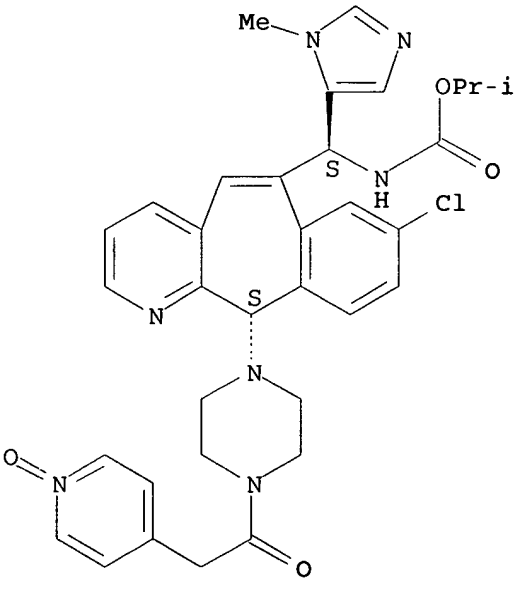
RN 740822-35-9 HCAPLUS
CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



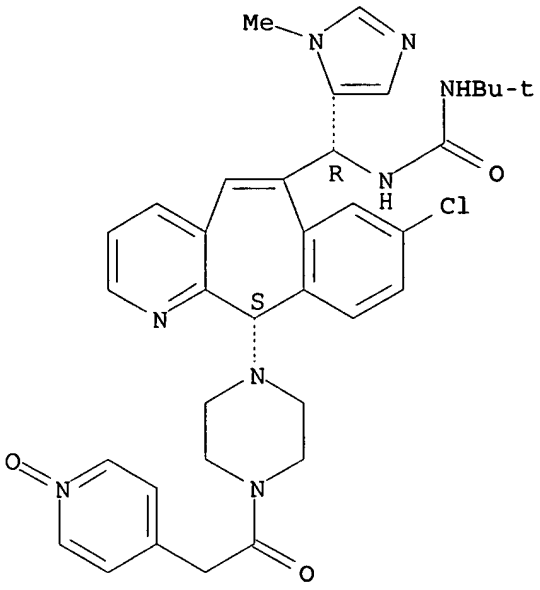
RN 740822-36-0 HCAPLUS
CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



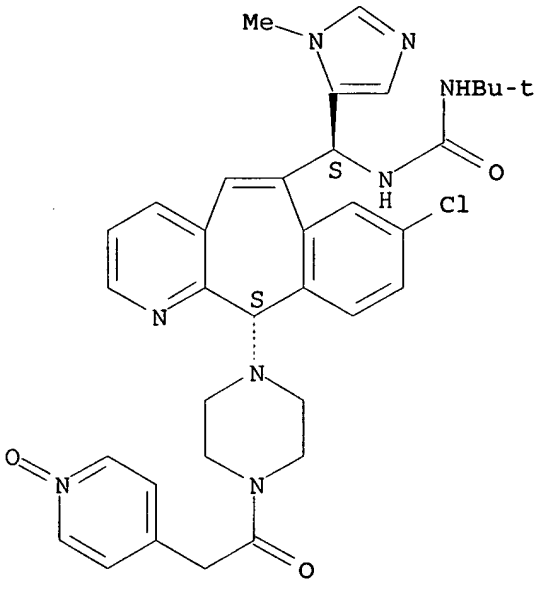
RN 740822-37-1 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 740822-38-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:559501 HCAPLUS
DOCUMENT NUMBER: 141:106498
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors
INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin,

John J.; Li, Ge; Huang, Chia-yu; James, Ray A.; Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004122018	A1	20040624	US 2002-325896	20021219
US 2002198216	A1	20021226	US 2001-940811	20010828
US 2003229099	A1	20031211	US 2002-85896	20020227
US 2004122018	A1	20040624	US 2002-325896	20021219

PRIORITY APPLN. INFO.:

US 2001-940811	A2	20010828
US 2002-85896	A2	20020227
US 2002-325896	A	20021219
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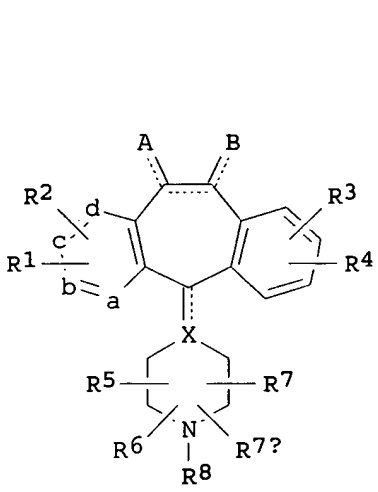
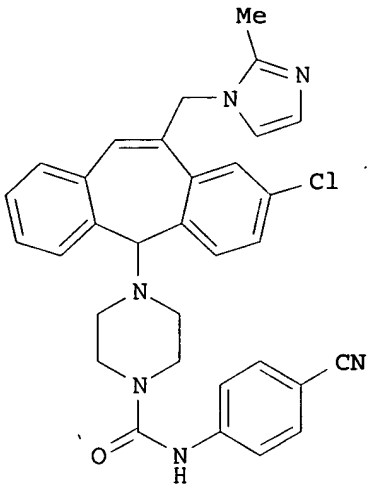


I



II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM

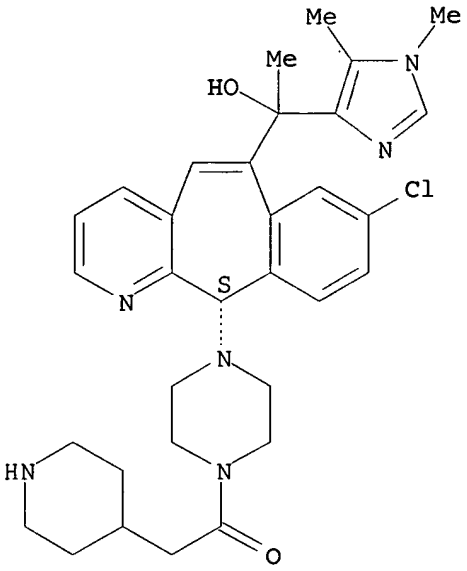
and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

IT 721435-94-5P 721435-95-6P 721436-05-1P
721436-06-2P 721437-03-2P 721437-04-3P
721437-14-5P 721437-15-6P 721437-95-2P
721437-96-3P 721438-06-8P 721438-07-9P
721438-90-0P 721438-91-1P 721439-01-6P
721439-02-7P 721439-82-3P 721439-83-4P
721439-93-6P 721439-94-7P 721440-80-8P
721440-81-9P 721440-91-1P 721440-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FPT inhibitor; preparation of tricyclic antitumor agents as farnesyl protein transferase inhibitors for treatment of cancer and other proliferative diseases)

RN 721435-94-5 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

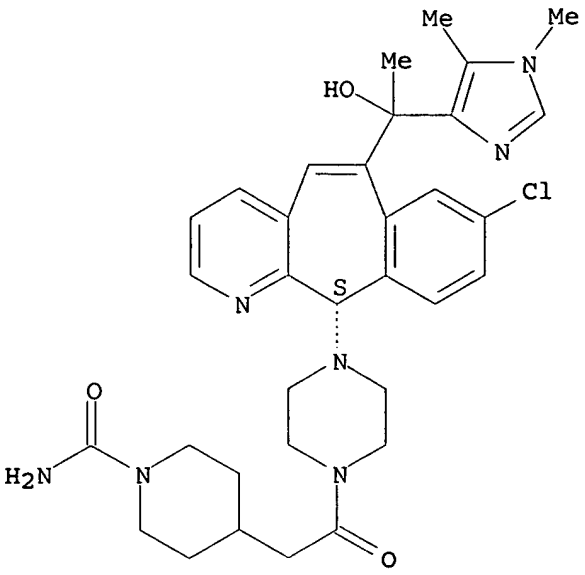
Absolute stereochemistry.



RN 721435-95-6 HCAPLUS

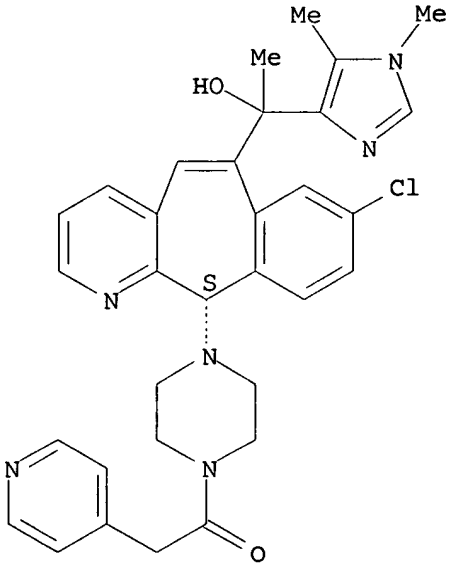
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



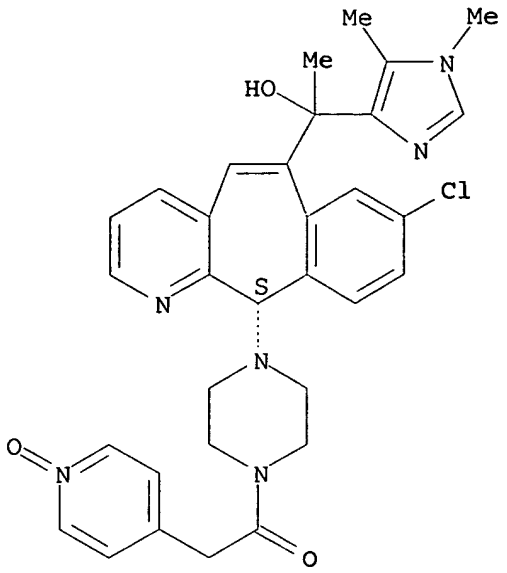
RN 721436-05-1 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



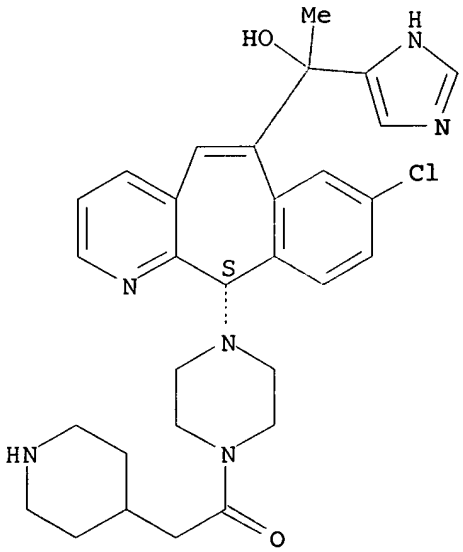
RN 721436-06-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



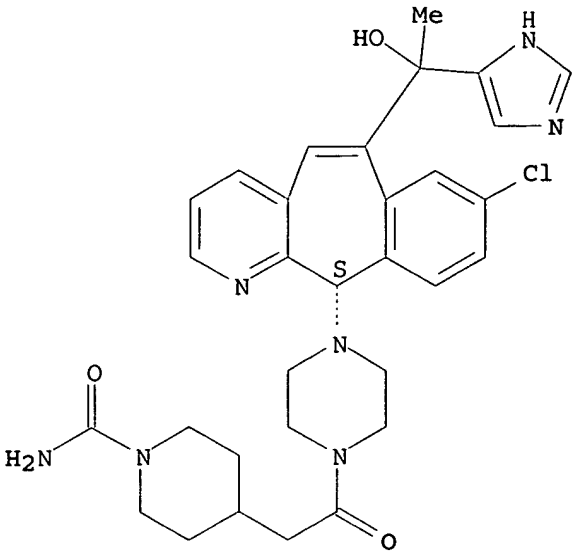
RN 721437-03-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



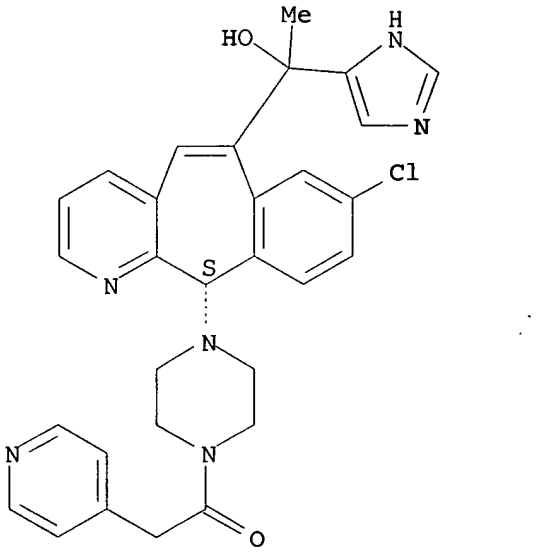
RN 721437-04-3 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



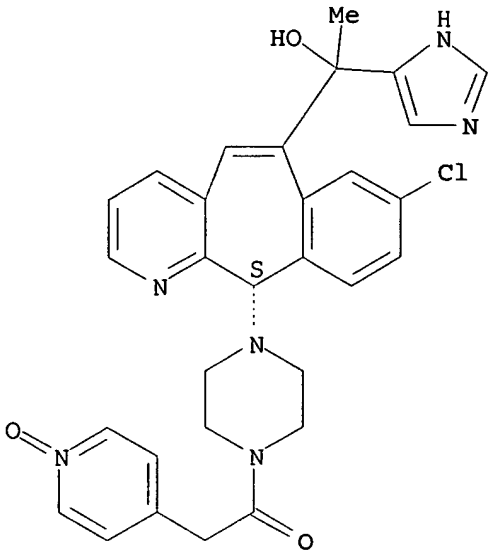
RN 721437-14-5 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



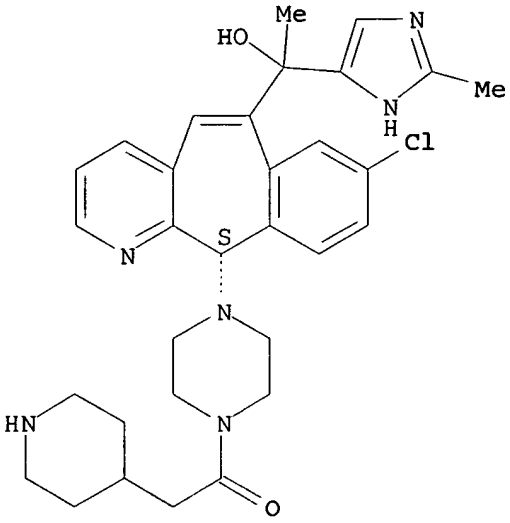
RN 721437-15-6 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



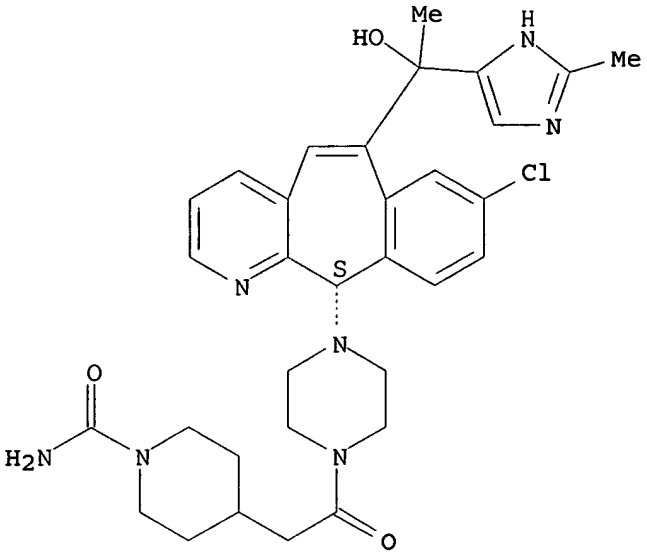
RN 721437-95-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



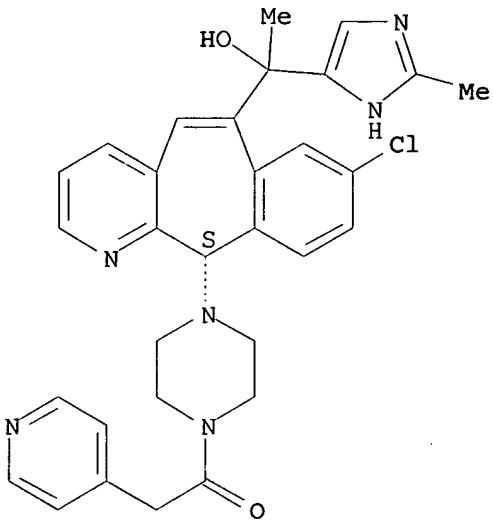
RN 721437-96-3 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



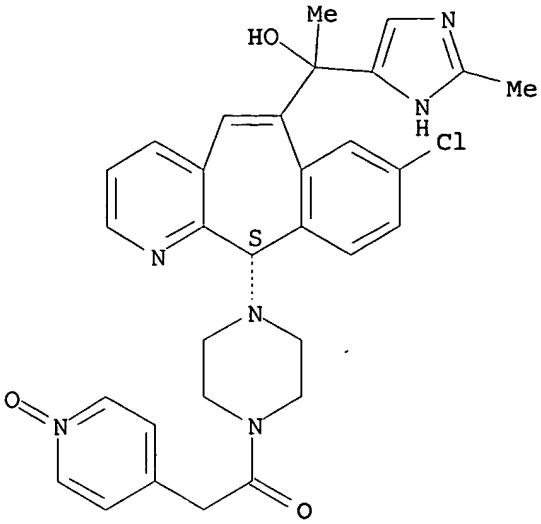
RN 721438-06-8 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



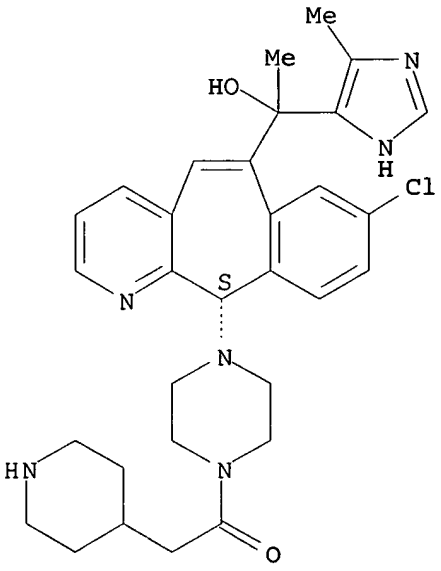
RN 721438-07-9 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



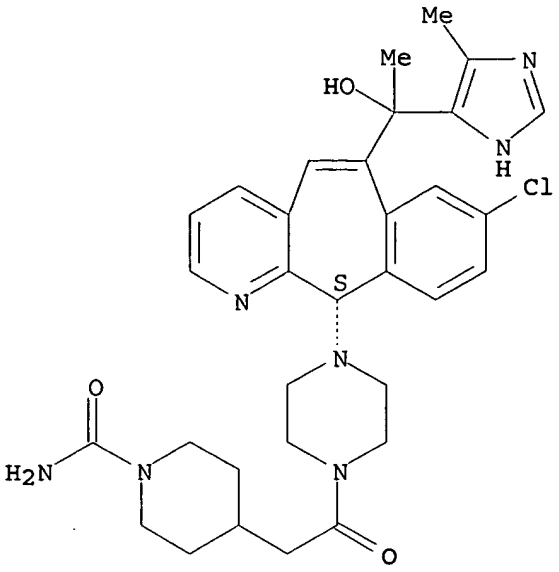
RN 721438-90-0 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



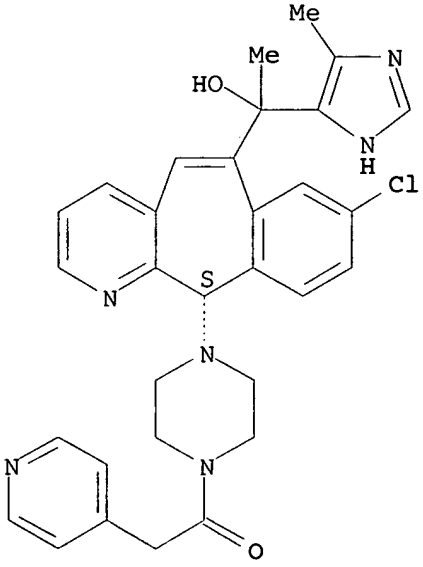
RN 721438-91-1 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



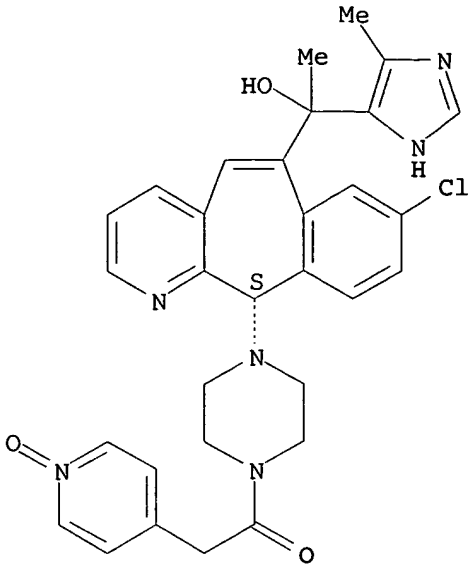
RN 721439-01-6 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



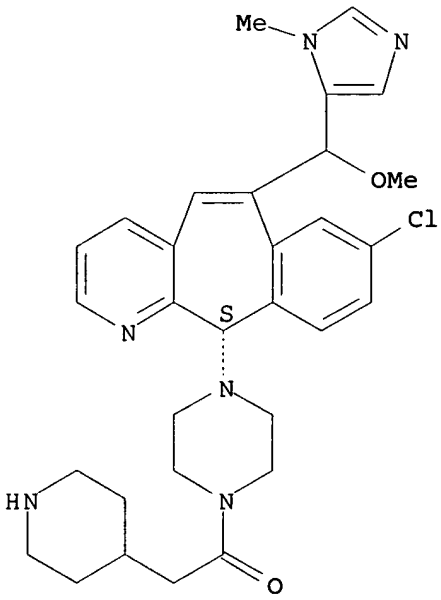
RN 721439-02-7 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



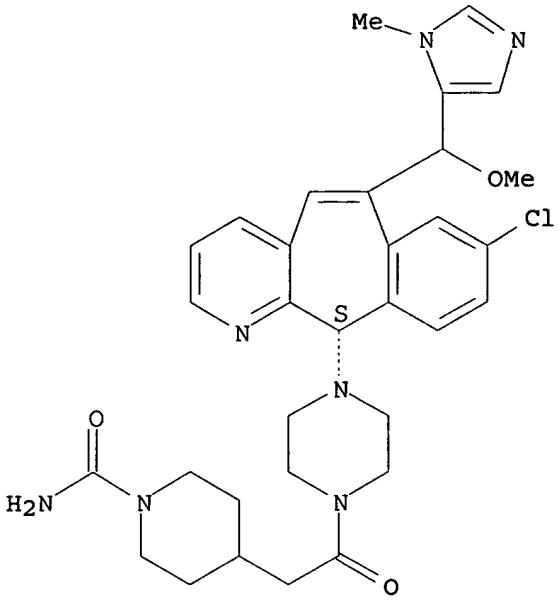
RN 721439-82-3 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



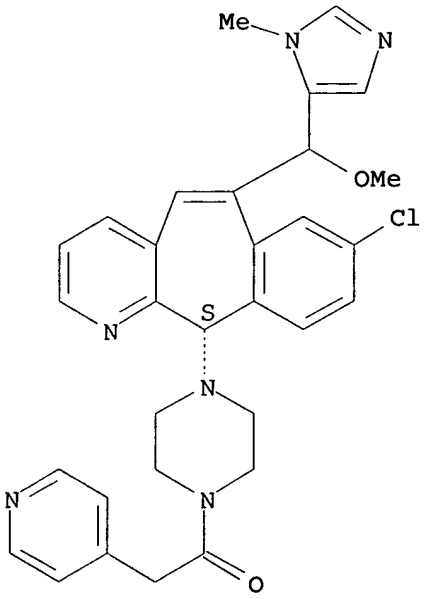
RN 721439-83-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



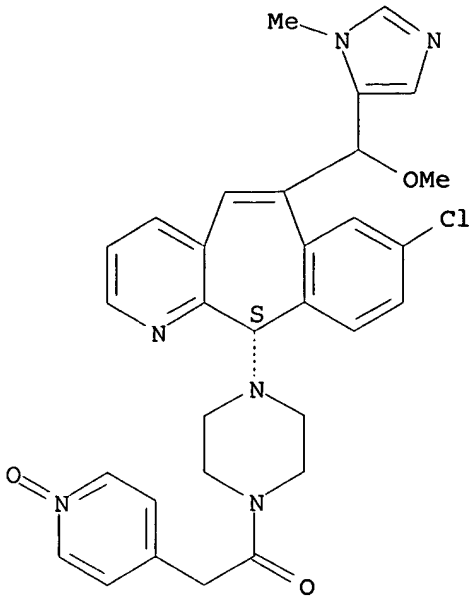
RN 721439-93-6 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



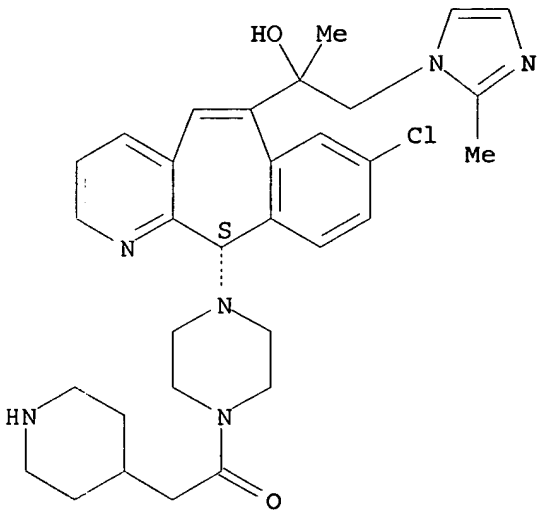
RN 721439-94-7 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



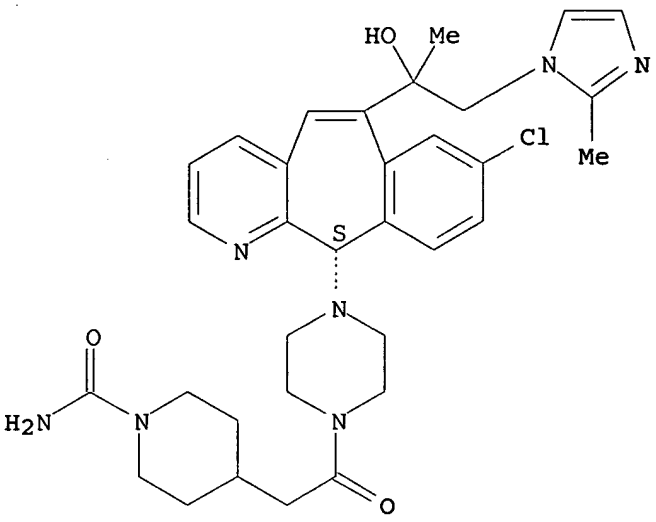
RN 721440-80-8 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



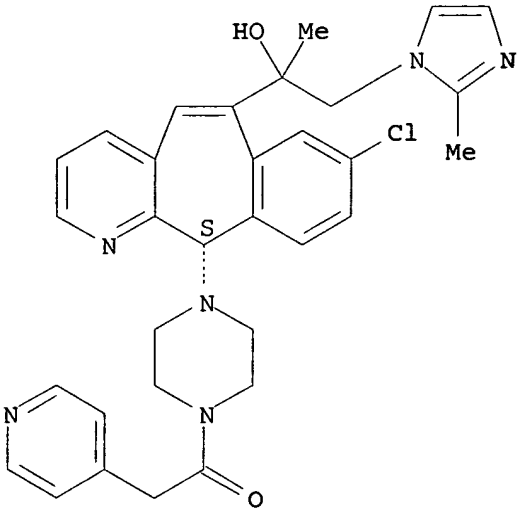
RN 721440-81-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 721440-91-1 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 721440-92-2 HCAPLUS
CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.